Q N N R ¹³	$ \begin{array}{c c} & & & \\ & & & &$	Q ()0-3 N N R ¹³
$ \begin{array}{cccccccccccccccccccccccccccccccccccc$	R ¹³ R ¹³ Q Q	$\begin{array}{c} & & & \\ & & \\ & & & \\ & & \\ & & & \\ & & & \\ & & \\ & & & \\ & & \\ & & & \\ & & \\ & & \\ & & & \\ & &$
$\begin{array}{c c} & & & \\ & & \\ & & & \\ & & & \\ & & & \\ & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ &$	N N R ¹³	Q N N R ¹³
R ¹³ () ¹⁻² () ⁰⁻³ ()	R ¹³ Q Q Q	R ¹³ () Q 0-4 N S N Q 0 0
R ¹³ () ₀₋₃ Q SH	R ¹³ () ₀₋₃ OH	R ¹³ () ₀₋₃ Q N H
N N R13	R ¹³ N O O R ¹³	N 10-2
O O 1-3 Q E Q	Q Q Q Q Q Q Q Q Q	O O R ¹³ S N 1-2 N Q R ¹³ O
$ \begin{array}{c} R^{13} \\ N \\ O \end{array} $ $ \begin{array}{c} O^{-2} \\ O \end{array} $ $ \begin{array}{c} C \\ O^{-4} \end{array} $	R ¹³ R ¹³ Q	R ¹³ Q Q Q Q Q Q Q Q Q Q Q Q Q Q Q Q Q Q Q

wherein wherein Q, R^{20} , and R^{13} are as defined above; each E is selected from -O-, -N(R^{13})-, -CH₂-, and -S(O)₀₋₂-; M is selected from -O-, -N(R^{13})-, -CH₂-, and -C(=O)N(R^{13})-; each V is independently either =N- or =C(H)-; each methylene in any of the above formulae is independently optionally substituted with R^{25} ; and R^{25} is selected from halogen, trihalomethyl, -CN, -NO₂, -NH₂, -OR³, -NR³R⁴, -S(O)₀₋₂R³, -SO₂NR³R³, -CO₂R³, -C(O)NR³R³, -N(R^3)SO₂R³, -N(R^3)C(O)R³, -N(R^3)CO₂R³, -C(O)R³, optionally substituted aryl, optionally substituted arylalkyl, heteroarylalkyl, and optionally substituted lower alkyl; two of R^{25} , together with the carbon or carbons to which they are attached, can combine to form a three- to seven-membered alicyclic or heteroalicyclic, two of R^{25} on a single carbon can be oxo.

4. The compound according to claim 3, wherein Ar is according to one of formula **IIa**, **IIb**, and **IIIa**.

$$(R^2)_{1-4}$$

$$(R^2)_{1-3}$$

$$(R^2)_{1-3}$$

$$(R^2)_{1-3}$$

$$(R^2)_{1-3}$$

$$(R^2)_{1-3}$$

- 5. The compound according to claim 4, wherein D is -O- and R^1 is -OR³.
- 6. The compound according to claim 5, wherein $-O-R^{50}$ and R^1 are interchangeably located at the 6-position and 7-position of the quinazoline or quinoline according to formula **I**.
- 7. The compound according to claim 6, wherein R^1 is -OH or -OC₁₋₆alkyl.
- 8. The compound according to claim 7, wherein A^1 is =N- or =C(H)-.
- 9. The compound according to claim 8, wherein G is selected from:

wherein Q, R^{20} , R^{13} , E, and R^{60} are as defined above; each methylene in any of the above formulae, other than those in a depicted ring, is independently optionally substituted with R^{25} ; and R^{25} is selected from halogen, trihalomethyl, oxo, -CN, -NO₂, -NH₂, -OR³, -NR³R⁴, -S(O)₀₋₂R³, -SO₂NR³R³, -CO₂R³, -C(O)NR³R³, -N(R³)SO₂R³, -N(R³)C(O)R³, -N(R³)CO₂R³, -C(O)R³, optionally substituted aryl, optionally substituted arylalkyl, heteroarylalkyl, and optionally substituted lower alkyl; two of R^{25} , together with the carbon or carbons to which they are attached, can combine to form a three- to seven-membered alicyclic or heteroalicyclic.

10. The compound according to claim 9, wherein Q is selected from:

$$(R^{20})_{0-4}$$
 P $(R^{20})_{0-4}$ $(R^{20})_{0-4}$

wherein R²⁰ is defined as above, and P is a five- to seven-membered ring, including the two shared carbons of the aromatic ring to which P is fused, P optionally containing between one and three heteroatoms.

11. The compound according to claim 10, wherein Ar is according to formula **Ha**, and G is selected from:

wherein Q, R^{20} , R^{13} , E, and R^{60} are as defined above, and each methylene in any of the above formulae, other than those in a depicted ring, is independently optionally substituted with R^{25} ; and R^{25} is selected from halogen, trihalomethyl, oxo, -CN, -NO₂, -NH₂, -OR³, -NR³R⁴, -S(O)₀₋₂R³, -SO₂NR³R³, -CO₂R³, -C(O)NR³R³, -N(R³)SO₂R³, -N(R³)C(O)R³, -N(R³)CO₂R³, -C(O)R³, optionally substituted aryl, optionally substituted arylalkyl, heteroarylalkyl, and optionally substituted lower alkyl; two of R^{25} , together with the carbon or carbons to which they are attached, can combine to form a three- to seven-membered alicyclic or heteroalicyclic.

12. The compound according to claim 10, wherein Ar is according to formula **IIb**, and G is selected from:

wherein Q, R²⁰, R¹³, E, and R⁶⁰ are as defined above, and each methylene in any of the above formulae, other than those depicted in a ring, is independently optionally substituted with R²⁵; and R²⁵ is selected from halogen, trihalomethyl, oxo, -CN, -NO₂, -NH₂, -OR³, -NR³R⁴, -S(O)₀₋₂R³, -SO₂NR³R³, -CO₂R³, -C(O)NR³R³, -N(R³)SO₂R³, -N(R³)C(O)R³, -N(R³)CO₂R³, -C(O)R³, optionally substituted aryl, optionally substituted arylalkyl, heteroarylalkyl, and optionally substituted lower alkyl; two of R²⁵, together with the carbon or carbons to which they are attached, can combine to form a three- to seven-membered alicyclic or heteroalicyclic.

- 13. The compound according to claim 12, wherein the methylene between the two carbonyls of the depicted formulae is di-substituted with either optionally substituted lower alkyl, or an optionally substituted spirocycle.
- 14. The compound according to claim 11 or claim 12, wherein R^{50} is a heteroalicylic or a C_{1-6} alkyl-heteroalicylic.
- 15. The compound according to claim 14, wherein at least one of R² is halogen.
- 16. The compound according to claim 14, wherein R^{50} is according to formula IV.
- 17. The compound according to claim 16, wherein the saturated bridged ring system according to formula **IV** has a geometry selected from the group consisting of [4.4.0], [4.3.0], [4.2.0], [4.1.0], [3.3.0], [3.2.0], [3.1.0], [3.3.3], [3.3.2], [3.3.1], [3.2.2], [3.2.1], [2.2.2], and [2.2.1].
- 18. The compound according to claim 17, wherein Y is selected from -CH₂CH₂CH₂-, -CH₂CH₂-, -CH₂CH₂-, -CH₂-, and absent.
- 19. The compound according to claim 18, wherein n is 0 and the saturated bridged ring system according to formula **IV** has a geometry selected from the group consisting of [4.4.0], [4.3.0], [4.2.0], [4.1.0], [3.3.0], [3.2.0], and [3.1.0].
- 20. The compound according to claim 19, wherein said saturated bridged ring system contains at least one annular nitrogen or at least one annular oxygen.
- 21. The compound according to claim 20, wherein said saturated bridged ring system contains $-NR^8$ -, wherein R^8 is selected from -H, optionally substituted lower alkyl, $-CO_2R^3$, $-C(O)NR^3R^3$, $-SO_2R^3$, and $-C(O)R^3$.

22. The compound according to claim 20, wherein said saturated bridged ring system is of formula **V**,

 \mathbf{v}

wherein U^1 is selected from -O-, -S(O)₀₋₂-, -NR⁸-, -CR⁶R⁷-, and absent; and e is 0 or 1.

- 23. The compound according to claim 22, wherein Y is -CH₂-.
- 24. The compound according to claim 23, wherein U^1 is -NR⁸-, wherein R⁸ is selected from -H, optionally substituted lower alkyl, -CO₂R³, -C(O)NR³R³, -SO₂R³, and -C(O)R³.
- 25. The compound according to claim 23, wherein U^1 is -O-.
- 26. The compound according to claim 23, wherein U¹ is absent.
- 27. The compound according to claim 20, wherein Y is selected from $-CH_2CH_2$ -, $-CH_2$ -, and absent.
- 28. The compound according to claim 27, wherein said saturated bridged ring system is of formula VI,

 \mathbf{VI}

wherein R⁹, R¹⁰, and R¹¹ are each independently selected from -H, and -OR¹²; or

- R^9 is selected from -H, and $-OR^{12}$, and R^{10} and R^{11} , when taken together, are either an optionally substituted alkylidene or an oxo;
- R¹² is selected from -H, -C(O)R³, optionally substituted lower alkylidyne, optionally substituted lower arylalkylidyne, optionally substituted lower heterocyclylalkylidyne, optionally substituted lower alkylidene, optionally

substituted lower alkylidenearyl, optionally substituted lower alkylideneheterocyclyl, optionally substituted lower alkyl, optionally substituted lower alkylaryl, optionally substituted aryl, optionally substituted lower heterocyclylalkyl, and optionally substituted heterocyclyl;

- or two R¹²'s, when taken together, form 1) a corresponding spirocyclic ketal when said two R¹²'s stem from R¹⁰ and R¹¹, or 2) a corresponding cyclic ketal when said two R¹²'s stem from R⁹ and one of R¹⁰ and R¹¹.
- 29. The compound according to claim 28, wherein one of R^{10} and R^{11} is $-OR^{12}$, wherein R^{12} is selected from -H, $-C(O)R^3$, and optionally substituted lower alkyl; and R^9 and the other of R^{10} and R^{11} are both -H.
- 30. The compound according to claim 29, wherein Y is either -CH₂- or absent.
- 31. The compound according to claim 30, wherein R⁹ is an alkyl group containing at least one fluorine substitution thereon.
- 32. The compound according to claim 21, wherein said saturated bridged ring system is of formula **VII**.

- 33. The compound according to claim 32, wherein Y is either -CH₂- or absent.
- 34. The compound according to claim 33, wherein R⁸ is methyl or ethyl.
- 35. The compound according to claim 21, wherein said saturated bridged ring system is of formula **VIII**.

- 36. The compound according to claim 35, wherein Y is -CH₂-.
- 37. The compound according to claim 36, wherein \mathbb{R}^8 is methyl or ethyl.

38. The compound according to claim 20, wherein said saturated bridged ring system is of formula **IX**

IX

wherein U^2 is selected from -O-, -S(O)₀₋₂-, -NR⁸-, -CR⁶R⁷-, and absent.

- 39. The compound according to claim 38, wherein R³ of formula **IX** is selected from -H and optionally substituted alkyl.
- 40. The compound according to claim 39, wherein U^2 is either $-CR^6R^7$ or absent.
- 41. The compound according to claim 40, wherein U² is either -CH₂- or absent.
- 42. The compound according to claim 41, wherein Y is -CH₂-.
- 43. The compound according to claim 21, wherein said saturated bridged ring system is according to formula **X**.

- 44. The compound according to claim 43, wherein \mathbb{R}^8 is methyl or ethyl.
- 45. The compound according to claim 1, selected from Table 1.

Table 1

Entry	Name	Structure
1		

Table 1

Entry	Name	Structure
1	N-[({3-fluoro-4-[(6- (methyloxy)-7-{[(3aR,6aS)- octahydrocyclopenta[c]pyrrol- 5-ylmethyl]oxy}quinazolin-4- yl)oxy]phenyl}amino)carbono thioyl]-2-phenylacetamide	
2	N-{[(3-fluoro-4-{[7- ({[(3aR,6aS)-2- methyloctahydrocyclopenta[c] pyrrol-5-yl]methyl}oxy)-6- (methyloxy)quinazolin-4- yl]oxy}phenyl)amino]carbono thioyl}-2-phenylacetamide	H N N N N N N N N N N N N N N N N N N N
3	N-{[(4-{[6,7-bis(methyloxy)quinolin-4-yl]oxy}-3-fluorophenyl)(methyl)amino]carbonothioyl}-2-phenylacetamide	S O N N N N N N N N N N N N N N N N N N
4	1-(4-{[6,7-bis(methyloxy)quinolin-4-yl]oxy}-3-fluorophenyl)imidazolidin-2-one	F NH
5	1-(4-{[6,7-bis(methyloxy)quinolin-4-yl]oxy}-3-fluorophenyl)-3-(phenylmethyl)imidazolidin-2-one	F N N
6	1-(4-{[6,7-bis(methyloxy)quinolin-4-yl]oxy}-3-fluorophenyl)-3-(phenylacetyl)imidazolidin-2-one	-O N N O N O

Table 1

Entry	Name	Structure
7	ethyl [(4-{[6,7-bis(methyloxy)quinolin-4-yl]oxy}-3-fluorophenyl)amino](oxo)acetate	F O O O NH O
8	N-{[(4-{[6,7-bis(methyloxy)quinazolin-4-yl]amino}-3-fluorophenyl)amino]carbonothioyl}-2-phenylacetamide	F S O S N H H
9	N'-(4-{[6,7-bis(methyloxy)quinolin-4-yl]oxy}-3-fluorophenyl)-N-methyl-N-(2-phenylethyl)sulfamide	F N S N N
10	N-(4-{[6,7-bis(methyloxy)quinolin-4-yl]oxy}-3-fluorophenyl)-3-(phenylmethyl)-1,2,4-oxadiazol-5-amine	F N N N N N N N N N N N N N N N N N N N
11	1-(4-{[6,7-bis(methyloxy)quinolin-4-yl]oxy}-3-fluorophenyl)piperidin-2-one	F N
12	N-(4-{[6,7-bis(methyloxy)quinolin-4-yl]oxy}-3-fluorophenyl)-N'-(phenylmethyl)ethanediamide	-o F O O NH HN-

Table 1

Entry	Name	Structure
13	N-(4-{[6,7-bis(methyloxy)quinolin-4-yl]oxy}-3-fluorophenyl)-4-phenyl-1,3-thiazol-2-amine	F S N N N N N N N N N N N N N N N N N N
14	N-(4-{[6,7-bis(methyloxy)quinolin-4-yl]oxy}-3-fluorophenyl)-N'-(2-phenylethyl)ethanediamide	-o NH HN-
15	N-(4-{[6,7-bis(methyloxy)quinolin-4-yl]oxy}-3-fluorophenyl)-1-phenylmethanesulfonamide	F O S O NH
16	N-(4-{[6,7-bis(methyloxy)quinolin-4-yl]oxy}-3-fluorophenyl)-2-phenylethanesulfonamide	NH ON SECOND
17	4-{[6,7-bis(methyloxy)quinolin-4-yl]oxy}-3-fluoro-N-(phenylmethyl)benzenesulfon amide	F O S NH
18	4-{[6,7-bis(methyloxy)quinolin-4-yl]oxy}-3-fluoro-N-methyl-N-(phenylmethyl)benzenesulfon amide	-0 F O S - N - N

Table 1

Entry	Name	Structure
19	4-{[6,7- bis(methyloxy)quinolin-4- yl]oxy}-3-fluoro-N-(2- phenylethyl)benzenesulfonam ide	-O S O S O S O O O O O O O O O O O O O O
20	4-{[6,7-bis(methyloxy)quinolin-4-yl]oxy}-3-fluoro-N-methyl-N-(2-phenylethyl)benzenesulfonamide	-0 - 0 - 0 - 0 - 0 - 0 - 0 - 0 - 0 - 0
21	4-{[6,7-bis(methyloxy)quinolin-4-yl]oxy}-3-fluoro-N-(3-phenylpropyl)benzenesulfonamide	P O S-NH
22	1-(4-{[6,7-bis(methyloxy)quinolin-4-yl]oxy}-3-fluorophenyl)pyrrolidin-2-one	F N
23	4-{[6,7-bis(methyloxy)quinolin-4-yl]oxy}phenyl (phenylmethyl)carbamate	ONH ONH
24	4-{[6,7- bis(methyloxy)quinolin-4- yl]oxy}phenyl (2- phenylethyl)carbamate	

Table 1

Entry	Name	Structure
25	4-{[6,7-bis(methyloxy)quinolin-4-yl]oxy}-3-fluoro-N-methyl-N-(3-phenylpropyl)benzenesulfonamide	-0 F O S N
26	N-(4-{[6,7-bis(methyloxy)quinolin-4-yl]oxy}-3-fluorophenyl)-N'-phenylethanediamide	N-NH HN-
27	N-{[(3-fluoro-4-{[7-{[(2-methyloctahydrocyclopenta[c] pyrrol-5-yl)methyl]oxy}-6-(methyloxy)quinolin-4-yl]oxy}phenyl)amino]carbono thioyl}-2-phenylacetamide	F S O S O S O S O S O S O S O S O S O S
28	N-[(Z)-[(4-{[6,7-bis(methyloxy)quinolin-4-yl]oxy}-3-fluorophenyl)amino](imino)methyl]-2-phenylacetamide	P NH O NH O NH
29	4-{[6,7-bis(methyloxy)quinolin-4-yl]oxy}-3-fluoro-N-[2-(phenyloxy)ethyl]benzenesulfonamide	F O S NH
30	N,N-(4-{[6,7-bis(methyloxy)quinolin-4-yl]oxy}-3-fluorophenyl)-bis-(3-phenylpropane-1-sulfonamide)	F O S O S O S O O S O O O O O O O O O O

Table 1

		Table 1
Entry	Name	Structure
31	N-(4-{[6,7-bis(methyloxy)quinolin-4-yl]oxy}-3-fluorophenyl)-3-phenylpropane-1-sulfonamide	-o NH ON NH
32	N2-[(4-{[6,7-bis(methyloxy)quinolin-4-yl]oxy}-3-fluorophenyl)sulfonyl]-N1-phenylglycinamide	F O S NH O HN
33	N-(6-{[6,7-bis(methyloxy)quinolin-4-yl]oxy}pyridin-3-yl)-2-phenylacetamide	
34	N-{[(6-{[6,7-bis(methyloxy)quinolin-4-yl]oxy}pyridin-3-yl)amino]carbonothioyl}-2-phenylacetamide	
35	6-{[6,7-bis(methyloxy)quinolin-4-yl]oxy}-1,3-benzothiazol-2-amine	N-N-N-N-N-N-N-N-N-N-N-N-N-N-N-N-N-N-N-
36	6-{[6,7-bis(methyloxy)quinolin-4-yl]oxy}-5-fluoro-1,3-benzothiazol-2-amine	S NH ₂

Table 1

Entry	Name	Structure
37	N-(6-{[6,7-bis(methyloxy)quinolin-4-yl]oxy}-5-fluoro-1,3-benzothiazol-2-yl)-2-phenylacetamide	-o S N O
38	N-(4-{[6,7-bis(methyloxy)quinolin-4-yl]oxy}-3-fluorophenyl)-N'-(2-morpholin-4-ylethyl)ethanediamide	NH HN NH HN
39	benzyl-{[4-(6,7-dimethoxy-quinolin-4-yloxy)-3-fluoro-phenylcarbamoyl]-methyl}-carbamic acid tert-butyl ester	F N N N N N N N N N N N N N N N N N N N
40	N1-(4-{[6,7-bis(methyloxy)quinolin-4-yl]oxy}-3-fluorophenyl)-N2-(phenylmethyl)glycinamide	
41	N2-acetyl-N1-(4-{[6,7-bis(methyloxy)quinolin-4-yl]oxy}-3-fluorophenyl)-N2-(phenylmethyl)glycinamide	F O O O O O O O O O O O O O O O O O O O
42	N-(6-{[6,7-bis(methyloxy)quinolin-4-yl]oxy}-1,3-benzothiazol-2-yl)-2-phenylacetamide	

Table 1

Entry	Name	Structure
43	benzyl-{[6-(6,7-dimethoxy-quinolin-4-yloxy)-pyridin-3-ylcarbamoyl]-methyl}-carbamic acid tert-butyl ester	
44	N1-(6-{[6,7-bis(methyloxy)quinolin-4-yl]oxy}pyridin-3-yl)-N2-(phenylmethyl)glycinamide	
45	N2-acetyl-N1-(6-{[6,7-bis(methyloxy)quinolin-4-yl]oxy}pyridin-3-yl)-N2-(phenylmethyl)glycinamide	
46	N-(6-{[6,7-bis(methyloxy)quinolin-4-yl]oxy}pyridin-3-yl)-3-phenylpropanamide	
47	N-(6-{[6,7-bis(methyloxy)quinolin-4-yl]oxy}pyridin-3-yl)-4-phenylbutanamide	
48	N1-(6-{[6,7-bis(methyloxy)quinolin-4-yl]oxy}pyridin-3-yl)-N2-methyl-N2-(phenylmethyl)glycinamide	

Table 1

Entry	Name	Structure
49	N-(4-{[6,7-bis(methyloxy)quinolin-4-yl]oxy}-3-fluorophenyl)-N'-{2-[4-(methyloxy)phenyl]ethyl}ethanediamide	-O NH HN-
50	N1-(4-{[6,7-bis(methyloxy)quinolin-4-yl]oxy}-3-fluorophenyl)-N2-methyl-N2-(phenylmethyl)glycinamide	F O N N N N N N N N N N N N N N N N N N
51	4-[(2-amino-1,3-benzothiazol-6-yl)oxy]-6,7-bis(methyloxy)-1-(2-oxo-2-phenylethyl)quinolinium	N+-
52	N-{[(4-{[6,7-bis(methyloxy)quinolin-4-yl]amino}phenyl)amino]carbonothioyl}-2-phenylacetamide	
53	N-(6-{[6,7-bis(methyloxy)quinolin-4-yl]oxy}-5-fluoro-1,3-benzothiazol-2-yl)-3-phenylpropanamide	
54	N-{[(6-{[6,7-bis(methyloxy)quinolin-4-yl]oxy}-5-chloropyridin-3-yl)amino]carbonothioyl}-2-phenylacetamide	

Table 1

		G
Entry	Name	Structure
55	N-(4-{[6,7-bis(methyloxy)quinolin-4-yl]oxy}-3-fluorophenyl)-N'-(2,3-dihydro-1H-inden-1-yl)ethanediamide	N-NH HN-
56	N-(4-{[6,7-bis(methyloxy)quinolin-4-yl]oxy}-3-fluorophenyl)-N'-(2,3-dihydro-1H-inden-2-yl)ethanediamide	NH HN
57	N-(4-{[6,7-bis(methyloxy)quinolin-4-yl]oxy}-3-fluorophenyl)-N'-(1,2,3,4-tetrahydronaphthalen-1-yl)ethanediamide	F O O NH HN
58	N'-(4-{[6,7-bis(methyloxy)quinolin-4-yl]oxy}-3-fluorophenyl)-N-(2-phenylethyl)-N-(phenylmethyl)sulfamide	-o NH O O S N
59	N1-(4-{[6,7-bis(methyloxy)quinolin-4-yl]oxy}-3-fluorophenyl)-N2-(trifluoroacetyl)glycinamide	P O HN F F
60	N-{[4-(6,7-dimethoxy-quinolin-4-yloxy)-3-fluoro-phenylcarbamoyl]-methyl}-benzamide	-o HN-O HN-O NH

Table 1

		Table 1
Entry	Name	Structure
61	N-(6-{[6,7-bis(methyloxy)quinolin-4-yl]oxy}pyridin-3-yl)-N'-(4-fluorophenyl)propanediamide	F O N N N N N N N N N N N N N N N N N N
62	N-(4-{[6,7-bis(methyloxy)quinolin-4-yl]oxy}-3-fluorophenyl)-N'-[(2S)-1,2,3,4-tetrahydronaphthalen-2-yl]ethanediamide	N-NH HN
63	N-(4-{[6,7- bis(methyloxy)quinolin-4- yl]oxy}-3-fluorophenyl)-N'- [2-(4- methylphenyl)ethyl]ethanedia mide	NH HN
64	N-(4-{[6,7-bis(methyloxy)quinolin-4-yl]oxy}-3-fluorophenyl)-N'-(2-phenylpropyl)ethanediamide	N-N-N-N-N-N-N-N-N-N-N-N-N-N-N-N-N-N-N-
65	N-(4-{[6,7-bis(methyloxy)quinolin-4-yl]oxy}-3-fluorophenyl)-N'- [2-(4-chlorophenyl)ethyl]ethanedia mide	NH HN—CI
66	N-(4-{[6,7-bis(methyloxy)quinolin-4-yl]oxy}-3-fluorophenyl)-N,N'-bis(phenylmethyl)sulfamide	F OS H

Table 1

Entry	Name	Structure
67	N-(4-{[6,7-bis(methyloxy)quinolin-4-yl]oxy}-3-fluorophenyl)-N,N'-bis(2-phenylethyl)sulfamide	-o F NH NH
68	ethyl [(6-{[6,7-bis(methyloxy)quinolin-4-yl]oxy}-5-chloropyridin-3-yl)amino](oxo)acetate	CI O O O NH O
69	N-(6-{[6,7-bis(methyloxy)quinolin-4-yl]oxy}-5-chloropyridin-3-yl)-N'-(2-phenylethyl)ethanediamide	CI O O O NH HN
70	N-(6-{[6,7-bis(methyloxy)quinolin-4-yl]oxy}-5-chloropyridin-3-yl)-N'-(4-fluorophenyl)propanediamide	CI N N N N N N N N N N N N N N N N N N N
71	N-(4-{[6,7-bis(methyloxy)quinolin-4-yl]oxy}-3-fluorophenyl)-N'-(1,2,3,4-tetrahydronaphthalen-2-yl)ethanediamide	F O O O O O O O O O O O O O O O O O O O
72	N-(4-{[6,7-bis(methyloxy)quinolin-4-yl]oxy}-3-fluorophenyl)-N'-[2-(1-methylpyrrolidin-2-yl)ethyl]ethanediamide	N-N-N-N-N-N-N-N-N-N-N-N-N-N-N-N-N-N-N-

Table 1

Entry	Name	Structure
73	N-(4-{[6,7-bis(methyloxy)quinolin-4-yl]oxy}-3-fluorophenyl)-N'-[2-(phenyloxy)ethyl]ethanediamide	P O O O NH HN
74	N-(4-{[6,7-bis(methyloxy)quinolin-4-yl]oxy}-3-fluorophenyl)-N'-[2-hydroxy-1-(phenylmethyl)ethyl]urea	
75	1-(4-{[6,7-bis(methyloxy)quinolin-4-yl]oxy}-3-fluorophenyl)-3-[(4-methylphenyl)sulfonyl]-4-(phenylmethyl)imidazolidin-2-one	
76	N'-(4-{[6,7-bis(methyloxy)quinolin-4-yl]oxy}-3-fluorophenyl)-N-methyl-N-(2-phenylethyl)ethanediamide	-o F O O NH N-
77	N-(4-{[6,7-bis(methyloxy)quinolin-4-yl]oxy}-3-fluorophenyl)-N'-{[3-(trifluoromethyl)phenyl]methyl}ethanediamide	P O O O NH HN F F
78	N-(4-{[6,7-bis(methyloxy)quinolin-4-yl]oxy}-3-fluorophenyl)-N'-{2-[3-(trifluoromethyl)phenyl]ethyl}ethanediamide	NH HN F F

Table 1

Entry	Name	Structure
Entry	Name	Structure
79	N-(6-{[6,7-bis(methyloxy)quinolin-4-yl]oxy}-5-chloropyridin-3-yl)-3-oxo-4-phenylbutanamide	CI N N N
80	N-(6-{[6,7-bis(methyloxy)quinolin-4-yl]oxy}-5-chloropyridin-3-yl)-2-[3-(trifluoromethyl)phenyl]acetamide	CI N N H F F
81	6-{[6,7-bis(methyloxy)quinolin-4-yl]oxy}-5-fluoro-N-[2-(phenyloxy)ethyl]-1,3-benzothiazol-2-amine	-o S N N
82	6-{[6,7-bis(methyloxy)quinolin-4-yl]oxy}-5-fluoro-N-(2-piperidin-1-ylethyl)-1,3-benzothiazol-2-amine	S H N
83	6-{[6,7-bis(methyloxy)quinolin-4-yl]oxy}-5-fluoro-N-methyl-N-(2-phenylethyl)-1,3-benzothiazol-2-amine	S N N
84	6-{[6,7-bis(methyloxy)quinolin-4-yl]oxy}-5-fluoro-N-(2-pyrrolidin-1-ylethyl)-1,3-benzothiazol-2-amine	

Table 1

Entry	Name	Structure
85	6-{[6,7-bis(methyloxy)quinolin-4-yl]oxy}-5-fluoro-N-{[3-(trifluoromethyl)phenyl]methyl}-1,3-benzothiazol-2-amine	S H F F F
86	6-{[6,7-bis(methyloxy)quinolin-4-yl]oxy}-5-fluoro-N-{2-[3-(trifluoromethyl)phenyl]ethyl}-1,3-benzothiazol-2-amine	
87	N-(6-{[6,7-bis(methyloxy)quinolin-4-yl]oxy}-5-chloropyridin-3-yl)-N'-[3-(trifluoromethyl)phenyl]propanediamide	CI N N N N N N N N N N N N N
88	N-(6-{[6,7-bis(methyloxy)quinolin-4-yl]oxy}-5-fluoro-1,3-benzothiazol-2-yl)-2-[3-(trifluoromethyl)phenyl]acetamide	
89	N1-(4-{[6,7-bis(methyloxy)quinolin-4-yl]oxy}-3-fluorophenyl)-N2-{[3-(trifluoromethyl)phenyl]methyl}glycinamide	F F F
90	N1-(4-{[6,7-bis(methyloxy)quinolin-4-yl]oxy}-3-fluorophenyl)-N2-(2-phenylethyl)glycinamide	F O HN

Table 1

Entry	Name	Structure
91	N1-(4-{[6,7-bis(methyloxy)quinolin-4-yl]oxy}-3-fluorophenyl)-N2-{2-[3-(trifluoromethyl)phenyl]ethyl}glycinamide	-O HN-FF
92	benzyl-{[5-chloro-6-(6,7-dimethoxy-quinolin-4-yloxy)-pyridin-3-ylcarbamoyl]-methyl}-carbamic acid tert-butyl ester	CI N N N N
93	N1-(6-{[6,7-bis(methyloxy)quinolin-4-yl]oxy}-5-chloropyridin-3-yl)-N2-(phenylmethyl)glycinamide	
94	N-(6-{[6,7-bis(methyloxy)quinolin-4-yl]oxy}-5-fluoro-1,3-benzothiazol-2-yl)-2-[3,5-bis(trifluoromethyl)phenyl]acetamide	-ON FFFFFFFFFFFFFFFFFFFFFFFFFFFFFFFFFFFF
95	N-(6-{[6,7-bis(methyloxy)quinolin-4-yl]oxy}-5-fluoro-1,3-benzothiazol-2-yl)-2-[2-chloro-5-(trifluoromethyl)phenyl]acetamide	-O S N CI F F
96	N-{3-fluoro-4-[(6- (methyloxy)-7-{[(1- methylpiperidin-4- yl)methyl]oxy}quinolin-4- yl)oxy]phenyl}-N'-(2- phenylethyl)ethanediamide	F O O O NH HN

Table 1

Entry	Name	Structure
97	N-(4-{[6,7-bis(methyloxy)quinolin-4-yl]oxy}-3-fluorophenyl)-N'-(1,2,3,4-tetrahydroisoquinolin-1-ylmethyl)ethanediamide	-O NH HN HN
98	N-(4-{[6,7-bis(methyloxy)quinolin-4-yl]oxy}-3-fluorophenyl)-N'-[(2-methyl-1,2,3,4-tetrahydroisoquinolin-1-yl)methyl]ethanediamide	N-NH HN
99	N1-(4-{[6,7-bis(methyloxy)quinolin-4-yl]oxy}-3-fluorophenyl)-N2-methyl-N2-{[3-(trifluoromethyl)phenyl]methyl}glycinamide	F N N N F F
100	N1-(4-{[6,7-bis(methyloxy)quinolin-4-yl]oxy}-3-fluorophenyl)-N2-methyl-N2-{2-[3-(trifluoromethyl)phenyl]ethyl}glycinamide	F O N F F F
101	N1-(4-{[6,7-bis(methyloxy)quinolin-4-yl]oxy}-3-fluorophenyl)-N2-methyl-N2-(2-phenylethyl)glycinamide	-o NH NH
102	1-(4-{[6,7-bis(methyloxy)quinolin-4-yl]oxy}-3-fluorophenyl)-4-(phenylmethyl)imidazolidin-2-one	F NH
103	N-(6-{[6,7-bis(methyloxy)quinolin-4-yl]oxy}pyridazin-3-yl)-N'-(4-fluorophenyl)propanediamide	F N N N N N N N N N N N N N N N N N N N

Table 1

Entry	Name	Structure
104	N-(6-{[6,7-bis(methyloxy)quinolin-4-yl]oxy}-5-chloropyridin-3-yl)-N'-(2-chlorophenyl)propanediamide	
105	N-(6-{[6,7-bis(methyloxy)quinolin-4-yl]oxy}-5-chloropyridin-3-yl)-N'-(3-chlorophenyl)propanediamide	CI N N N N N N CI
106	N1-(6-{[6,7-bis(methyloxy)quinolin-4-yl]oxy}-5-chloropyridin-3-yl)-N2-methyl-N2-(phenylmethyl)glycinamide	
107	N-(6-{[6,7-bis(methyloxy)quinolin-4-yl]oxy}-5-chloropyridin-3-yl)-N'-(4-chlorophenyl)propanediamide	CI N N N N N N N N N N N
108	(2E)-N-(4-{[6,7-bis(methyloxy)quinolin-4-yl]oxy}phenyl)-2-[(methyloxy)imino]propanamide	ONH N-O
109	(2E)-N-(4-{[6,7-bis(methyloxy)quinolin-4-yl]oxy}phenyl)-2-[(ethyloxy)imino]propanamid	O NH N-O

Table 1

	NT	Structure
Entry	Name	Structure
110	(2E)-N-(4-{[6,7-bis(methyloxy)quinolin-4-yl]oxy}phenyl)-2-{[(phenylmethyl)oxy]imino}propanamide	ON NH N-O
111	N-(4-{[6,7-bis(methyloxy)quinolin-4-yl]oxy}phenyl)-1-(phenylmethyl)prolinamide	
112	1-(4-{[6,7-bis(methyloxy)quinolin-4-yl]oxy}phenyl)-3-[(4-methylphenyl)sulfonyl]-4-(phenylmethyl)imidazolidin-2-one	
113	1-(4-{[6,7-bis(methyloxy)quinolin-4-yl]oxy}phenyl)-4-(phenylmethyl)imidazolidin-2-one	-0 N-N-NH
114	N-(4-{[6,7-bis(methyloxy)quinolin-4-yl]oxy}phenyl)-4-(phenylmethyl)-4,5-dihydro-1,3-oxazol-2-amine	
115	6,7-bis(methyloxy)-4-({4-[4-(qhenylmethyl)piperazin-1-yl]phenyl}oxy)quinoline	

Table 1

Entry	Name	Structure
116	1-(4-{[6,7-bis(methyloxy)quinolin-4-yl]oxy}phenyl)-4-(phenylmethyl)piperazin-2-one	
117	N1-(4-{[6,7-bis(methyloxy)quinolin-4-yl]oxy}phenyl)-N2-(phenylmethyl)alaninamide	ON NH HN
118	N1-(4-{[6,7-bis(methyloxy)quinolin-4-yl]oxy}phenyl)-N2-methyl-N2-(phenylmethyl)alaninamide	O NH N-
119	N1-(4-{[6,7-bis(methyloxy)quinolin-4-yl]oxy}phenyl)-N2-(phenylmethyl)leucinamide	O NH HN
120	N1-(4-{[6,7-bis(methyloxy)quinolin-4-yl]oxy}phenyl)-N2-methyl-N2-(phenylmethyl)leucinamide	-o NH N
121	N1-(4-{[6,7-bis(methyloxy)quinolin-4-yl]oxy}phenyl)-N2-(phenylmethyl)valinamide	O NH HN

Table 1

Entry	Name	Structure
122	4-(6,7-dimethoxy-quinolin-4-ylamino)-N-(3-phenyl-propyl)-benzamide	
123	4-benzyl-1-[4-(6,7-dimethoxy-quinolin-4-yloxy)-phenyl]-tetrahydro-pyrimidin-2-one	N N N N N N N N N N N N N N N N N N N
124	N-{3-Fluoro-4-[6-methoxy-7- (piperidin-4-ylmethoxy)- quinolin-4-yloxy]-phenyl}-N'- phenethyl-oxalamide	F O O O O O O O O O O O O O O O O O O O
125	2-(Benzyl-methyl-amino)-N- [4-(6,7-dimethoxy-quinolin-4- yloxy)-phenyl]-3-methyl- butyramide (note: Alphabetic order of prefixes ignored while selecting parent chain)	
126	N-[4-(6,7-Dimethoxy-quinolin-4-yloxy)-phenyl]-2-phenoxyimino-propionamide	

Table 1

Entry	Name	Structure
127	2-Benzyloxyimino-N-[4-(6,7-dimethoxy-quinolin-4-yloxy)-phenyl]-2-phenyl-acetamide	
128	4-[4-(4-Benzyl-piperidin-1- yl)-phenoxy]-6,7-dimethoxy- quinoline	
129	N-[4-(6,7-Dimethoxy-quinolin-4-yloxy)-3-fluoro-phenyl]-N'-(2-isopropyl-1,2,3,4-tetrahydro-isoquinolin-1-ylmethyl)-oxalamide	F O O O O O O O O O O O O O O O O O O O
130	N-[4-(6,7-Dimethoxy-quinolin-4-yloxy)-3-fluoro-phenyl]-N'-(2-ethyl-1,2,3,4-tetrahydro-isoquinolin-1-ylmethyl)-oxalamide	F O H HN N

Table 1

Entry	Name	Structure
131	4-(4-{3-Chloro-5-[2-(4-fluoro-phenylcarbamoyl)-acetylamino]-pyridin-2-yloxy}-6-methoxy-quinolin-7-yloxymethyl)-piperidine-1-carboxylic acid tert-butyl ester	
132	N-{5-Chloro-6-[6-methoxy-7- (piperidin-4-ylmethoxy)- quinolin-4-yloxy]-pyridin-3- yl}-N'-(4-fluoro-phenyl)- malonamide	
133	N-{5-Chloro-6-[6-methoxy-7- (1-methyl-piperidin-4- ylmethoxy)-quinolin-4- yloxy]-pyridin-3-yl}-N'-(4- fluoro-phenyl)-malonamide	
134	N-{4-[7-(3-Diethylamino- propoxy)-6-methoxy- quinolin-4-yloxy]-3-fluoro- phenyl}-N'-phenethyl- oxalamide	

Table 1

Entry	Name	Structure
135	N-{3-Fluoro-4-[6-methoxy-7- (3-morpholin-4-yl-propoxy)- quinolin-4-yloxy]-phenyl}-N'- phenethyl-oxalamide	
136	N-{3-Fluoro-4-[6-methoxy-7-(3-piperidin-1-yl-propoxy)-quinolin-4-yloxy]-phenyl}-N'-phenethyl-oxalamide	
137	N-{4-[7-(2-Diethylamino- ethoxy)-6-methoxy-quinolin- 4-yloxy]-3-fluoro-phenyl}-N'- phenethyl-oxalamide	
138	N-{3-Fluoro-4-[6-methoxy-7- (1-methyl-piperidin-4- ylmethoxy)-quinolin-4- yloxy]-phenyl}-N'-methyl-N'- phenethyl-oxalamide	

Table 1

Entry	Name	Structure
139	N-{3-Fluoro-4-[6-methoxy-7- (2-methyl-octahydro- cyclopenta[c]pyrrol-5- ylmethoxy)-quinolin-4- yloxy]-phenyl}-N'-phenethyl- oxalamide	
140	N-{3-Fluoro-4-[6-methoxy-7- (2-methyl-octahydro- cyclopenta[c]pyrrol-5- ylmethoxy)-quinazolin-4- yloxy]-phenyl}-N'-phenethyl- oxalamide	
141	2-(3,4-Dihydro-1H- isoquinolin-2-yl)-N-{3-fluoro- 4-[6-methoxy-7-(1-methyl- piperidin-4-ylmethoxy)- quinolin-4-yloxy]-phenyl}-2- oxo-acetamide	
142	N-{3-Fluoro-4-[6-methoxy-7- (piperidin-4-ylmethoxy)- quinolin-4-yloxy]-phenyl}-2- oxo-2-(3-phenyl-pyrrolidin-1- yl)-acetamide	

Table 1

Entry	Name	Structure
143	N-{3-Fluoro-4-[6-methoxy-7- (piperidin-4-ylmethoxy)- quinolin-4-yloxy]-phenyl}-2- oxo-2-(2-phenyl-morpholin-4- yl)-acetamide	
144	N-(2-Dimethylamino-2-phenyl-ethyl)-N'-{3-fluoro-4-[6-methoxy-7-(piperidin-4-ylmethoxy)-quinolin-4-yloxy]-phenyl}-oxalamide	
145	N-{3-Fluoro-4-[6-methoxy-7- (piperidin-4-ylmethoxy)- quinolin-4-yloxy]-phenyl}-N'- (2-oxo-2-phenyl-ethyl)- oxalamide	F S H
146	N-[5-Chloro-6-(6,7-dimethoxy-quinolin-4-yloxy)-pyridin-3-yl]-2,2-difluoro-N'-(4-fluoro-phenyl)-malonamide	

Table 1

Entry	Name	Structure
147	N-Benzyl-N'-{3-fluoro-4-[6- methoxy-7-(1-methyl- piperidin-4-ylmethoxy)- quinolin-4-yloxy]-phenyl}- oxalamide	F O O O O O O O O O O O O O O O O O O O
148	N-{3-Fluoro-4-[6-methoxy-7- (piperidin-4-ylmethoxy)- quinolin-4-yloxy]-phenyl}-N'- [2-(2-fluoro-phenyl)-ethyl]- oxalamide	
149	N-[2-(3-Chloro-phenyl)- ethyl]-N'-{3-fluoro-4-[6- methoxy-7-(piperidin-4- ylmethoxy)-quinolin-4- yloxy]-phenyl}-oxalamide	
150	N-{3-Fluoro-4-[6-methoxy-7- (piperidin-4-ylmethoxy)- quinolin-4-yloxy]-phenyl}-N'- [2-(2-methoxy-phenyl)-ethyl]- oxalamide	F N HN

Table 1

Entry	Name	Structure
151	N-{3-Fluoro-4-[6-methoxy-7- (piperidin-4-ylmethoxy)- quinolin-4-yloxy]-phenyl}-N'- (2-pyridin-3-yl-ethyl)- oxalamide	F N HN N
152	N-Benzyl-N'-{3-fluoro-4-[6- methoxy-7-(piperidin-4- ylmethoxy)-quinolin-4- yloxy]-phenyl}-oxalamide	
153	N-[2-(2,5-Dimethoxy- phenyl)-ethyl]-N'-{3-fluoro-4- [6-methoxy-7-(piperidin-4- ylmethoxy)-quinolin-4- yloxy]-phenyl}-oxalamide	
154	N-{3-Fluoro-4-[6-methoxy-7- (piperidin-4-ylmethoxy)- quinolin-4-yloxy]-phenyl}-N'- [2-(2-trifluoromethyl-phenyl)- ethyl]-oxalamide	F HN F F

Table 1

Entry	Name	Structure
155	N-[2-(2-Ethoxy-phenyl)-ethyl]-N'-{3-fluoro-4-[6-methoxy-7-(piperidin-4-ylmethoxy)-quinolin-4-yloxy]-phenyl}-oxalamide	F N H N H N H N H N H N H N H N H N H N
156	N-[2-(2,4-Dimethyl-phenyl)- ethyl]-N'-{3-fluoro-4-[6- methoxy-7-(piperidin-4- ylmethoxy)-quinolin-4- yloxy]-phenyl}-oxalamide	NH NHN HN
157	N-{3-Fluoro-4-[6-methoxy-7- (piperidin-4-ylmethoxy)- quinolin-4-yloxy]-phenyl}-N'- (1S -phenyl-2-p-tolyl-ethyl)- oxalamide	
158	N-[2-(4-Chloro-phenyl)- ethyl]-N'-{3-fluoro-4-[6- methoxy-7-(piperidin-4- ylmethoxy)-quinolin-4- yloxy]-phenyl}-oxalamide	CI C

Table 1

Entry	Name	Structure
159	N-{3-Fluoro-4-[6-methoxy-7- (1-methyl-piperidin-4- ylmethoxy)-quinolin-4- yloxy]-phenyl}-oxalamic acid	N OH
160	N-{3-Fluoro-4-[6-methoxy-7- (piperidin-4-ylmethoxy)- quinolin-4-yloxy]-phenyl}-N'- [2-(3-fluoro-phenyl)-ethyl]- oxalamide	F O HE F
161	N-[2-(2-Chloro-phenyl)- ethyl]-N'-{3-fluoro-4-[6- methoxy-7-(piperidin-4- ylmethoxy)-quinolin-4- yloxy]-phenyl}-oxalamide	
162	N-{3-Fluoro-4-[6-methoxy-7- (piperidin-4-ylmethoxy)- quinolin-4-yloxy]-phenyl}-N'- [2-(3-methoxy-phenyl)-ethyl]- oxalamide	PH OF HE OF

Table 1

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Entry	Name	Structure
163	N-(1,2-Diphenyl-ethyl)-N'-{3- fluoro-4-[6-methoxy-7- (piperidin-4-ylmethoxy)- quinolin-4-yloxy]-phenyl}- oxalamide	
164	N-[2-(2,4-Dichloro-phenyl)- ethyl]-N'-{3-fluoro-4-[6- methoxy-7-(piperidin-4- ylmethoxy)-quinolin-4- yloxy]-phenyl}-oxalamide	CI C
165	N-[2-(3,4-Dimethoxy-phenyl)-ethyl]-N'-{3-fluoro-4-[6-methoxy-7-(piperidin-4-ylmethoxy)-quinolin-4-yloxy]-phenyl}-oxalamide	F HN HN
166	N-[2-(4-Ethyl-phenyl)-ethyl]- N'-{3-fluoro-4-[6-methoxy-7- (piperidin-4-ylmethoxy)- quinolin-4-yloxy]-phenyl}- oxalamide	

Table 1

Entry	Name	Structure
167	N-[2-(4-Ethoxy-phenyl)- ethyl]-N'-{3-fluoro-4-[6- methoxy-7-(piperidin-4- ylmethoxy)-quinolin-4- yloxy]-phenyl}-oxalamide	
168	N-[2-(4-Ethoxy-3-methoxy-phenyl)-ethyl]-N'-{3-fluoro-4-[6-methoxy-7-(piperidin-4-ylmethoxy)-quinolin-4-yloxy]-phenyl}-oxalamide	
169	N-{3-Fluoro-4-[6-methoxy-7- (piperidin-4-ylmethoxy)- quinolin-4-yloxy]-phenyl}-N'- [2-(4-phenoxy-phenyl)-ethyl]- oxalamide	

Table 1

Entry	Name	Structure
170	N-[2-(3-Ethoxy-4-methoxy-phenyl)-ethyl]-N'-{3-fluoro-4-[6-methoxy-7-(piperidin-4-ylmethoxy)-quinolin-4-yloxy]-phenyl}-oxalamide	
171	N-{3-Fluoro-4-[6-methoxy-7- (piperidin-4-ylmethoxy)- quinolin-4-yloxy]-phenyl}-N'- (2-pyridin-2-yl-ethyl)- oxalamide	F N H N N N N N N N N N N N N N N N N N
172	N-{3-Fluoro-4-[6-methoxy-7- (piperidin-4-ylmethoxy)- quinolin-4-yloxy]-phenyl}-N'- (2-pyridin-4-yl-ethyl)- oxalamide	
173	N-{3-Fluoro-4-[6-methoxy-7- (piperidin-4-ylmethoxy)- quinolin-4-yloxy]-phenyl}-N'- [2-(4-fluoro-phenyl)-ethyl]- oxalamide	F F

Table 1

Entry	Name	Structure
174	N-[2-(2-Bromo-phenyl)- ethyl]-N'-{3-fluoro-4-[6- methoxy-7-(piperidin-4- ylmethoxy)-quinolin-4- yloxy]-phenyl}-oxalamide	PH O HN Br
175	N-[2-(2-Chloro-6-fluoro-phenyl)-ethyl]-N'-{3-fluoro-4-[6-methoxy-7-(piperidin-4-ylmethoxy)-quinolin-4-yloxy]-phenyl}-oxalamide	F CI
176	N-{3-Fluoro-4-[6-methoxy-7- (piperidin-4-ylmethoxy)- quinolin-4-yloxy]-phenyl}-N'- (2 <i>R</i> -phenyl-propyl)-oxalamide	
177	N-{3-Fluoro-4-[6-methoxy-7- (piperidin-4-ylmethoxy)- quinolin-4-yloxy]-phenyl}-N'- indan-1-yl-oxalamide	

Table 1

Entry	Name	Structure
178	N-{3-Fluoro-4-[6-methoxy-7- (1-methyl-piperidin-4- ylmethoxy)-quinolin-4- yloxy]-phenyl}-N'-isobutyl- oxalamide	F O O O O O O O O O O O O O O O O O O O
179	N-{3-Fluoro-4-[6-methoxy-7- (1-methyl-piperidin-4- ylmethoxy)-quinolin-4- yloxy]-phenyl}-N'-(3-methyl- butyl)-oxalamide	F O D D D D D D D D D D D D D D D D D D
180	N-{3-Fluoro-4-[6-methoxy-7- (1-methyl-piperidin-4- ylmethoxy)-quinolin-4- yloxy]-phenyl}-N'-(2 <i>R</i> - phenyl-propyl)-oxalamide	F O O O O O O O O O O O O O O O O O O O
181	N-{3-Fluoro-4-[6-methoxy-7- (1-methyl-piperidin-4- ylmethoxy)-quinolin-4- yloxy]-phenyl}-N'-(2-phenyl- propyl)-oxalamide	

Table 1

		Table 1
Entry	Name	Structure
182	N-{3-Fluoro-4-[6-methoxy-7- (1-methyl-piperidin-4- ylmethoxy)-quinolin-4- yloxy]-phenyl}-N'-indan-2-yl- oxalamide	
183	N-{3-Fluoro-4-[6-methoxy-7- (piperidin-4-ylmethoxy)- quinolin-4-yloxy]-phenyl}-N'- (1 <i>R</i> -phenyl-ethyl)-oxalamide	F N HN HN
184	N-{3-Fluoro-4-[6-methoxy-7- (piperidin-4-ylmethoxy)- quinolin-4-yloxy]-phenyl}-N'- (1S-phenyl-ethyl)-oxalamide	N HN HN
185	N-[2-(3-Bromo-phenyl)-ethyl]-N'-{3-fluoro-4-[6-methoxy-7-(piperidin-4-ylmethoxy)-quinolin-4-yloxy]-phenyl}-oxalamide	Br NH

Table 1

Entry	Name	Structure
186	N-[2-(2,6-Dichloro-phenyl)- ethyl]-N'-{3-fluoro-4-[6- methoxy-7-(piperidin-4- ylmethoxy)-quinolin-4- yloxy]-phenyl}-oxalamide	
187	N-[2-(2,4-Dichloro-phenyl)- ethyl]-N'-{3-fluoro-4-[6- methoxy-7-(piperidin-4- ylmethoxy)-quinolin-4- yloxy]-phenyl}-oxalamide	L CI
188	N-(2-Benzo[1,3]dioxol-5-yl- ethyl)-N'-{3-fluoro-4-[6- methoxy-7-(piperidin-4- ylmethoxy)-quinolin-4- yloxy]-phenyl}-oxalamide	
189	N-[2-(3-Bromo-4-methoxy-phenyl)-ethyl]-N'-{3-fluoro-4-[6-methoxy-7-(piperidin-4-ylmethoxy)-quinolin-4-yloxy]-phenyl}-oxalamide	F O O O O O O O O O O O O O O O O O O O

Table 1

Entry	Name	Structure
190	N-[2-(3,5-Dimethoxy-phenyl)-ethyl]-N'-{3-fluoro-4-[6-methoxy-7-(piperidin-4-ylmethoxy)-quinolin-4-yloxy]-phenyl}-oxalamide	
191	N-{3-Fluoro-4-[6-methoxy-7- (piperidin-4-ylmethoxy)- quinolin-4-yloxy]-phenyl}-N'- (2-o-tolyl-ethyl)-oxalamide	
192	N-{3-Fluoro-4-[6-methoxy-7- (piperidin-4-ylmethoxy)- quinolin-4-yloxy]-phenyl}-N'- (2-m-tolyl-ethyl)-oxalamide	P N N N N N N N N N N N N N N N N N N N

Table 1

Entry	Name	Structure
193	N-[2-(3-Ethoxy-phenyl)- ethyl]-N'-{3-fluoro-4-[6- methoxy-7-(piperidin-4- ylmethoxy)-quinolin-4- yloxy]-phenyl}-oxalamide	
194	N-[2-(3,4-Dimethyl-phenyl)- ethyl]-N'-{3-fluoro-4-[6- methoxy-7-(piperidin-4- ylmethoxy)-quinolin-4- yloxy]-phenyl}-oxalamide	
195	N-[2-(2,5-Dimethyl-phenyl)- ethyl]-N'-{3-fluoro-4-[6- methoxy-7-(piperidin-4- ylmethoxy)-quinolin-4- yloxy]-phenyl}-oxalamide	
196	N-[2-(3-Chloro-4-propoxy-phenyl)-ethyl]-N'-{3-fluoro-4-[6-methoxy-7-(piperidin-4-ylmethoxy)-quinolin-4-yloxy]-phenyl}-oxalamide	F O H NH CI

Table 1

Entry	Name	Structure
197	N-[2-(4-Butoxy-3-chloro-phenyl)-ethyl]-N'-{3-fluoro-4-[6-methoxy-7-(piperidin-4-ylmethoxy)-quinolin-4-yloxy]-phenyl}-oxalamide	L CI NH NH
198	N-[2-(4-tert-Butyl-phenyl)- ethyl]-N'-{3-fluoro-4-[6- methoxy-7-(piperidin-4- ylmethoxy)-quinolin-4- yloxy]-phenyl}-oxalamide	F N N N N N N N N N N N N N N N N N N N
199	N-{3-Fluoro-4-[6-methoxy-7- (piperidin-4-ylmethoxy)- quinolin-4-yloxy]-phenyl}-N'- [2-(4-sulfamoyl-phenyl)- ethyl]-oxalamide	H ₂ N _N S

Table 1

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Entry	Name	Structure
200	N-{3-Fluoro-4-[6-methoxy-7- (piperidin-4-ylmethoxy)- quinolin-4-yloxy]-phenyl}-N'- [2-(4-hydroxy-3-methoxy- phenyl)-ethyl]-oxalamide	N N N N N N N N N N N N N N N N N N N
201	N-{3-Fluoro-4-[6-methoxy-7- (piperidin-4-ylmethoxy)- quinolin-4-yloxy]-phenyl}-N'- [2-(3-hydroxy-4-methoxy- phenyl)-ethyl]-oxalamide	F O O NH NH HO NH
202	N-(2,4-Dichloro-benzyl)-N'- {3-fluoro-4-[6-methoxy-7- (piperidin-4-ylmethoxy)- quinolin-4-yloxy]-phenyl}- oxalamide	

Table 1

Entry	Name	Structure
203	N-{3-Fluoro-4-[6-methoxy-7- (piperidin-4-ylmethoxy)- quinolin-4-yloxy]-phenyl}-N'- (4-fluoro-2-trifluoromethyl- benzyl)-oxalamide	F N N N F F F
204	N-{3-Fluoro-4-[6-methoxy-7- (piperidin-4-ylmethoxy)- quinolin-4-yloxy]-phenyl}-N'- (1-p-tolyl-ethyl)-oxalamide	
205	N-{3-Fluoro-4-[6-methoxy-7- (piperidin-4-ylmethoxy)- quinolin-4-yloxy]-phenyl}-N'- (3-fluoro-4-trifluoromethyl- benzyl)-oxalamide	F CF ₃

Table 1

Entry	Name	Structure
206	N-(3-Chloro-4-fluoro-benzyl)- N'-{3-fluoro-4-[6-methoxy-7- (piperidin-4-ylmethoxy)- quinolin-4-yloxy]-phenyl}- oxalamide	F O H O H
207	N-{3-Fluoro-4-[6-methoxy-7- (piperidin-4-ylmethoxy)- quinolin-4-yloxy]-phenyl}-N'- [1-(3-methoxy-phenyl)-ethyl]- oxalamide	
208	N-{3-Fluoro-4-[6-methoxy-7- (piperidin-4-ylmethoxy)- quinolin-4-yloxy]-phenyl}-N'- (1-naphthalen-2-yl-ethyl)- oxalamide	

Table 1

Entry	Name	Structure
- Intily	TAILLE	Suuciule
209	N-(4-Chloro-3- trifluoromethyl-benzyl)-N'- {3-fluoro-4-[6-methoxy-7- (piperidin-4-ylmethoxy)- quinolin-4-yloxy]-phenyl}- oxalamide	F ₃ C CI
210	N-{3-Fluoro-4-[6-methoxy-7- (piperidin-4-ylmethoxy)- quinolin-4-yloxy]-phenyl}-N'- (1-p-tolyl-ethyl)-oxalamide	
211	N-{3-Fluoro-4-[6-methoxy-7- (piperidin-4-ylmethoxy)- quinolin-4-yloxy]-phenyl}-N'- (6-trifluoromethyl-pyridin-3- ylmethyl)-oxalamide	F O DH O DH O CF3

Table 1

Entry	Name	Structure
212	N-{3-Fluoro-4-[6-methoxy-7- (piperidin-4-ylmethoxy)- quinolin-4-yloxy]-phenyl}-N'- (2-methyl-benzyl)-oxalamide	
213	N-{3-Fluoro-4-[6-methoxy-7- (piperidin-4-ylmethoxy)- quinolin-4-yloxy]-phenyl}-N'- (3-methyl-benzyl)-oxalamide	
214	N-{3-Fluoro-4-[6-methoxy-7- (piperidin-4-ylmethoxy)- quinolin-4-yloxy]-phenyl}-N'- (4-fluoro-3-trifluoromethyl- benzyl)-oxalamide	F ₃ C F
215	N-(3,5-Dichloro-benzyl)-N'- {3-fluoro-4-[6-methoxy-7- (piperidin-4-ylmethoxy)- quinolin-4-yloxy]-phenyl}- oxalamide	F O O O O O O O O O O O O O O O O O O O

Table 1

Entry	Name	Structure
216	N-{3-Fluoro-4-[6-methoxy-7- (piperidin-4-ylmethoxy)- quinolin-4-yloxy]-phenyl}-N'- (1R,2,3,4-tetrahydro- naphthalen-1-yl)-oxalamide	
217	N-{3-Fluoro-4-[6-methoxy-7- (piperidin-4-ylmethoxy)- quinolin-4-yloxy]-phenyl}-N'- (1S,2,3,4-tetrahydro- naphthalen-1-yl)-oxalamide	
218	N-Cyclopentyl-N'-{3-fluoro- 4-[6-methoxy-7-(piperidin-4- ylmethoxy)-quinolin-4- yloxy]-phenyl}-oxalamide	F NH NH
219	N-[1-(4-Bromo-phenyl)- ethyl]-N'-{3-fluoro-4-[6- methoxy-7-(piperidin-4- ylmethoxy)-quinolin-4- yloxy]-phenyl}-oxalamide	F O NH

Table 1

Entry	Name	Structure
220	N-(2-Fluoro-benzyl)-N'-{3- fluoro-4-[6-methoxy-7- (piperidin-4-ylmethoxy)- quinolin-4-yloxy]-phenyl}- oxalamide	F N N N N N N N N N N N N N N N N N N N
221	N-[2-(3,4-Dichloro-phenyl)- ethyl]-N'-{3-fluoro-4-[6- methoxy-7-(piperidin-4- ylmethoxy)-quinolin-4- yloxy]-phenyl}-oxalamide	
222	N-(4-Fluoro-benzyl)-N'-{3- fluoro-4-[6-methoxy-7- (piperidin-4-ylmethoxy)- quinolin-4-yloxy]-phenyl}- oxalamide	
223	N-(2,3-Difluoro-benzyl)-N'- {3-fluoro-4-[6-methoxy-7- (piperidin-4-ylmethoxy)- quinolin-4-yloxy]-phenyl}- oxalamide	F F

Table 1

Entry	Name	Structure
224	N-{3-Fluoro-4-[6-methoxy-7- (piperidin-4-ylmethoxy)- quinolin-4-yloxy]-phenyl}-N'- (2-phenoxy-ethyl)-oxalamide	
225	N-(2,2-Diphenyl-ethyl)-N'-{3- fluoro-4-[6-methoxy-7- (piperidin-4-ylmethoxy)- quinolin-4-yloxy]-phenyl}- oxalamide	
226	N-{3-Fluoro-4-[6-methoxy-7- (piperidin-4-ylmethoxy)- quinolin-4-yloxy]-phenyl}-N'- [2-(4-methoxy-phenyl)-ethyl]- oxalamide	
227	N-{3-Fluoro-4-[6-methoxy-7- (piperidin-4-ylmethoxy)- quinolin-4-yloxy]-phenyl}-N'- (2-phenyl-propyl)-oxalamide	

Table 1

Entry	Name	Structure
228	N-[2-(4-Bromo-phenyl)- ethyl]-N'-{3-fluoro-4-[6- methoxy-7-(piperidin-4- ylmethoxy)-quinolin-4- yloxy]-phenyl}-oxalamide	F O O O O O O O O O O O O O O O O O O O
229	N-{4-[7-(1-Ethyl-piperidin-4-ylmethoxy)-6-methoxy-quinolin-4-yloxy]-3-fluoro-phenyl}-2-oxo-2-(2-phenyl-morpholin-4-yl)-acetamide	
230	N-{3-Fluoro-4-[6-methoxy-7- (piperidin-4-ylmethoxy)- quinolin-4-yloxy]-phenyl}-N'- (3-fluoro-5-trifluoromethyl- benzyl)-oxalamide	F ₃ C F
231	N-(3,5-Difluoro-benzyl)-N'- {3-fluoro-4-[6-methoxy-7- (piperidin-4-ylmethoxy)- quinolin-4-yloxy]-phenyl}- oxalamide	F F

Table 1

Entry	Name	Structure
232	N-(2-Chloro-5- trifluoromethyl-benzyl)-N'- {3-fluoro-4-[6-methoxy-7- (piperidin-4-ylmethoxy)- quinolin-4-yloxy]-phenyl}- oxalamide	F ₃ C Ci
233	N-[4-(6,7-Dimethoxy-quinolin-4-yloxy)-3-fluoro-phenyl]-N'-(2-dimethylamino-2-phenyl-ethyl)-oxalamide	F O D D D D D D D D D D D D D D D D D D
234	N-{3-Fluoro-4-[6-methoxy-7- (piperidin-4-ylmethoxy)- quinolin-4-yloxy]-phenyl}-N'- (4-methoxy-benzyl)- oxalamide	

Table 1

Entry	Name	Structure
235	N-{3-Fluoro-4-[6-methoxy-7- (piperidin-4-ylmethoxy)- quinolin-4-yloxy]-phenyl}-N'- (4-trifluoromethyl-benzyl)- oxalamide	F O O O O O O O O O O O O O O O O O O O
236	N-{3-Fluoro-4-[6-methoxy-7- (piperidin-4-ylmethoxy)- quinolin-4-yloxy]-phenyl}-N'- (3-methoxy-benzyl)- oxalamide	
237	N-{3-Fluoro-4-[6-methoxy-7- (piperidin-4-ylmethoxy)- quinolin-4-yloxy]-phenyl}-N'- (3-trifluoromethyl-benzyl)- oxalamide	F ₃ C
238	N-{3-Fluoro-4-[6-methoxy-7- (piperidin-4-ylmethoxy)- quinolin-4-yloxy]-phenyl}-N'- (3-trifluoromethoxy-benzyl)- oxalamide	F ₃ C ₀

Table 1

Entry	Name	Structure
239	N-{3-Fluoro-4-[6-methoxy-7- (piperidin-4-ylmethoxy)- quinolin-4-yloxy]-phenyl}-N'- (2-methoxy-benzyl)- oxalamide	
240	N-{3-Fluoro-4-[6-methoxy-7- (piperidin-4-ylmethoxy)- quinolin-4-yloxy]-phenyl}-N'- (2-trifluoromethyl-benzyl)- oxalamide	
241	N-(3-Chloro-benzyl)-N'-{3- fluoro-4-[6-methoxy-7- (piperidin-4-ylmethoxy)- quinolin-4-yloxy]-phenyl}- oxalamide	F O D D D D D D D D D D D D D D D D D D
242	N-{3-Fluoro-4-[6-methoxy-7- (piperidin-4-ylmethoxy)- quinolin-4-yloxy]-phenyl}-N'- (2-trifluoromethoxy-benzyl)- oxalamide	F ₃ C

Table 1

Entry	Name	Structure
243	N-(2-Chloro-benzyl)-N'-{3- fluoro-4-[6-methoxy-7- (piperidin-4-ylmethoxy)- quinolin-4-yloxy]-phenyl}- oxalamide	L O H CI
244	N-{3-Fluoro-4-[6-methoxy-7- (piperidin-4-ylmethoxy)- quinolin-4-yloxy]-phenyl}-N'- (4-trifluoromethoxy-benzyl)- oxalamide	F ₃ C.
245	N-{3-Fluoro-4-[6-methoxy-7- (1-methyl-piperidin-4- ylmethoxy)-quinolin-4- yloxy]-phenyl}-N'-(4- methoxy-benzyl)-oxalamide	F ON NH NH

Table 1

Entry	Name	Structure
246	N-{3-Fluoro-4-[6-methoxy-7- (1-methyl-piperidin-4- ylmethoxy)-quinolin-4- yloxy]-phenyl}-N'-(4- trifluoromethyl-benzyl)- oxalamide	F O O O O O O O O O O O O O O O O O O O
247	N-{4-[7-(Azetidin-3- ylmethoxy)-6-methoxy- quinolin-4-yloxy]-3-fluoro- phenyl}-N'-phenethyl- oxalamide	
248	N-{3-Fluoro-4-[6-methoxy-7- (1-methyl-azetidin-3- ylmethoxy)-quinolin-4- yloxy]-phenyl}-N'-phenethyl- oxalamide	F ON NH
249	N-{3-Fluoro-4-[6-methoxy-7- (piperidin-4-ylmethoxy)- quinolin-4-yloxy]-phenyl}-N'- (2-hydroxy-2-phenyl-ethyl)- oxalamide	F OH OH

Table 1

Entry	Name	Structure
250	N-[5-Chloro-6-(6,7-dimethoxy-quinolin-4-yloxy)-pyridin-3-yl]-N'-(2,4-difluoro-phenyl)-malonamide	
251	N-[5-Chloro-6-(6,7-dimethoxy-quinolin-4-yloxy)-pyridin-3-yl]-N'-(4-fluoro-phenyl)-N'-methyl-malonamide	
252	N-{3-Fluoro-4-[6-methoxy-7- (piperidin-4-ylmethoxy)- quinolin-4-yloxy]-phenyl}-N'- (1R-phenyl-propyl)- oxalamide	

Table 1

Entry	Name	Structure
253	N-{3-Fluoro-4-[6-methoxy-7- (piperidin-4-ylmethoxy)- quinolin-4-yloxy]-phenyl}-N'- (1R-phenyl-propyl)- oxalamide	F N N N N N N N N N N N N N N N N N N N
254	N-(3,4-Difluoro-benzyl)-N'- {3-fluoro-4-[6-methoxy-7- (piperidin-4-ylmethoxy)- quinolin-4-yloxy]-phenyl}- oxalamide	F ON NH NH NH NH
255	N-(2,6-Difluoro-benzyl)-N'- {3-fluoro-4-[6-methoxy-7- (piperidin-4-ylmethoxy)- quinolin-4-yloxy]-phenyl}- oxalamide	
256	N-{3-Fluoro-4-[6-methoxy-7- (1-methyl-piperidin-4- ylmethoxy)-quinolin-4- yloxy]-phenyl}-N'-[2-(4- fluoro-phenyl)-ethyl]- oxalamide	F NH

Table 1

Entry	Name	Structure
257	N-{3-Fluoro-4-[6-methoxy-7- (1-methyl-piperidin-4- ylmethoxy)-quinolin-4- yloxy]-phenyl}-N'-phenyl- oxalamide	F O D D D D D D D D D D D D D D D D D D
258	N-{3-Fluoro-4-[6-methoxy-7- (piperidin-4-ylmethoxy)- quinolin-4-yloxy]-phenyl}-N'- (3-fluoro-phenyl)-oxalamide	
259	N-(4-Chloro-3-fluoro- phenyl)-N'-{3-fluoro-4-[6- methoxy-7-(piperidin-4- ylmethoxy)-quinolin-4- yloxy]-phenyl}-oxalamide	
260	N-(3,4-Dimethoxy-phenyl)- N'-{3-fluoro-4-[6-methoxy-7- (piperidin-4-ylmethoxy)- quinolin-4-yloxy]-phenyl}- oxalamide	F O NH

Table 1

Entry	Name	Structure
261	N-{3-Fluoro-4-[6-methoxy-7- (piperidin-4-ylmethoxy)- quinolin-4-yloxy]-phenyl}-N'- (3-methyl-butyl)-oxalamide	
262	N-(3,3-Dimethyl-butyl)-N'- {3-fluoro-4-[6-methoxy-7- (piperidin-4-ylmethoxy)- quinolin-4-yloxy]-phenyl}- oxalamide	
263	N-{5-Chloro-6-[6-methoxy-7-(3-piperidin-1-yl-propoxy)-quinolin-4-yloxy]-pyridin-3-yl}-N'-(4-fluoro-phenyl)-malonamide	
264	N-{5-Chloro-6-[6-methoxy-7- (3-morpholin-4-yl-propoxy)- quinolin-4-yloxy]-pyridin-3- yl}-N'-(4-fluoro-phenyl)- malonamide	

Table 1

Γ		Table 1
Entry	Name	Structure
265	N-{5-Chloro-6-[7-(3-diethylamino-propoxy)-6-methoxy-quinolin-4-yloxy]-pyridin-3-yl}-N'-(4-fluoro-phenyl)-malonamide	C O N HN O F
266	N-(4-Chloro-benzyl)-N'-{3-fluoro-4-[6-methoxy-7-(piperidin-4-ylmethoxy)-quinolin-4-yloxy]-phenyl}-oxalamide	F O O O O O O O O O O O O O O O O O O O
267	N-(3,5-Dimethoxy-benzyl)- N'-{3-fluoro-4-[6-methoxy-7- (piperidin-4-ylmethoxy)- quinolin-4-yloxy]-phenyl}- oxalamide	

Table 1

Entry	Name	Structure
268	N-(4-Butyl-benzyl)-N'-{3- fluoro-4-[6-methoxy-7- (piperidin-4-ylmethoxy)- quinolin-4-yloxy]-phenyl}- oxalamide	
269	N-{3-Fluoro-4-[6-methoxy-7- (piperidin-4-ylmethoxy)- quinolin-4-yloxy]-phenyl}-N'- (2-p-tolyl-ethyl)-oxalamide	
270	N-(3,5-Bis-trifluoromethyl-benzyl)-N'-{3-fluoro-4-[6-methoxy-7-(piperidin-4-ylmethoxy)-quinolin-4-yloxy]-phenyl}-oxalamide	F ₃ C CF ₃

Table 1

Entry	Name	Structure
271	N-{3-Fluoro-4-[6-methoxy-7- (piperidin-4-ylmethoxy)- quinolin-4-yloxy]-phenyl}-N'- pyrazin-2-ylmethyl-oxalamide	
272	N-{3-Fluoro-4-[6-methoxy-7- (piperidin-4-ylmethoxy)- quinolin-4-yloxy]-phenyl}-N'- pyridin-2-ylmethyl-oxalamide	
273	N-{3-Fluoro-4-[6-methoxy-7- (piperidin-4-ylmethoxy)- quinazolin-4-yloxy]-phenyl}- N'-phenethyl-oxalamide	
274	N-{3-Fluoro-4-[6-methoxy-7- (1-methyl-piperidin-4- ylmethoxy)-quinazolin-4- yloxy]-phenyl}-N'-phenethyl- oxalamide	F O O O O O O O O O O O O O O O O O O O

Table 1

Entry	Name	Structure
275	N-{3-Fluoro-4-[6-methoxy-7- (piperidin-4-ylmethoxy)- quinolin-4-yloxy]-phenyl}-N'- (2-fluoro-3-trifluoromethyl- benzyl)-oxalamide	F ₃ C
276	N-[2-(2-Bromo-6-methoxy-phenyl)-ethyl]-N'-{3-fluoro-4-[6-methoxy-7-(piperidin-4-ylmethoxy)-quinolin-4-yloxy]-phenyl}-oxalamide	P O D D D D D D D D D D D D D D D D D D
277	N-[2-(3,4-Dimethoxy-phenyl)-ethyl]-N'-{3-fluoro-4-[6-methoxy-7-(piperidin-4-ylmethoxy)-quinolin-4-yloxy]-phenyl}-N-methyloxalamide	
278	N-[2-(5-Bromo-2-methoxy-phenyl)-ethyl]-N'-{3-fluoro-4-[6-methoxy-7-(piperidin-4-ylmethoxy)-quinolin-4-yloxy]-phenyl}-oxalamide	P O O O O O O O O O O O O O O O O O O O

Table 1

Entry	Name	Structure
279	N-{3-Fluoro-4-[6-methoxy-7- (piperidin-4-ylmethoxy)- quinolin-4-yloxy]-phenyl}-N'- (2-fluoro-5-trifluoromethyl- benzyl)-oxalamide	F CF ₃
280	N-{3-Fluoro-4-[6-methoxy-7- (piperidin-4-ylmethoxy)- quinolin-4-yloxy]-phenyl}-N'- [1-(4-fluoro-phenyl)-ethyl]- oxalamide	
281	N-(1S-Benzyl-2-oxo-2-pyrrolidin-1-yl-ethyl)-N'-{3-fluoro-4-[6-methoxy-7-(piperidin-4-ylmethoxy)-quinolin-4-yloxy]-phenyl}-oxalamide	F N HN N N
282	N-{3-Fluoro-4-[6-methoxy-7- (octahydro- cyclopenta[c]pyrrol-5- ylmethoxy)-quinazolin-4- yloxy]-phenyl}-N'-phenethyl- oxalamide	H N N N N N N N N N N N N N N N N N N N

Table 1

Entry	Name	Structure
283	N-[2-(4-Amino-phenyl)- ethyl]-N'-{3-fluoro-4-[6- methoxy-7-(piperidin-4- ylmethoxy)-quinolin-4- yloxy]-phenyl}-oxalamide	H ₂ N
284	2-(4-Benzyl-piperidin-1-yl)- N-{3-fluoro-4-[6-methoxy-7- (piperidin-4-ylmethoxy)- quinolin-4-yloxy]-phenyl}-2- oxo-acetamide	
285	N-[4-(6,7-Dimethoxy-quinolin-4-yloxy)-phenyl]-N'-(4-fluoro-phenyl)-malonamide	

Table 1

Entry	Name	Structure
286	N-[5-Chloro-6-(6,7-dimethoxy-quinolin-4-yloxy)-pyridin-3-yl]-N'-(3-fluoro-phenyl)-malonamide	
287	N-[5-Chloro-6-(6,7- dimethoxy-quinolin-4-yloxy)- pyridin-3-yl]-N'-phenyl- malonamide	
288	N-[5-Chloro-6-(6,7-dimethoxy-quinolin-4-yloxy)-pyridin-3-yl]-N'-(4-fluoro-phenyl)-2,2-dimethyl-malonamide	
289	N-Ethyl-N'-{3-fluoro-4-[6- methoxy-7-(piperidin-4- ylmethoxy)-quinolin-4- yloxy]-phenyl}-oxalamide	

Table 1

Entry	Name	Structure
290	N-{3-Fluoro-4-[6-methoxy-7- (piperidin-4-ylmethoxy)- quinolin-4-yloxy]-phenyl}-N'- isopropyl-oxalamide	F ON NH NH
291	N-Butyl-N'-{3-fluoro-4-[6-methoxy-7-(piperidin-4-ylmethoxy)-quinolin-4-yloxy]-phenyl}-oxalamide	
292	N-{3-Fluoro-4-[6-methoxy-7- (piperidin-4-ylmethoxy)- quinolin-4-yloxy]-phenyl}-N'- (2-methoxy-ethyl)-oxalamide	
293	N-Cyclopropylmethyl-N'-{3-fluoro-4-[6-methoxy-7-(piperidin-4-ylmethoxy)-quinolin-4-yloxy]-phenyl}-oxalamide	F N N N N N N N N N N N N N N N N N N N
294	N-{3-Fluoro-4-[6-methoxy-7- (piperidin-4-ylmethoxy)- quinolin-4-yloxy]-phenyl}-N'- (2-morpholin-4-yl-ethyl)- oxalamide	

Table 1

Entry	Name	Structure
295	N-{3-Fluoro-4-[6-methoxy-7- (piperidin-4-ylmethoxy)- quinolin-4-yloxy]-phenyl}-2- oxo-2-pyrrolidin-1-yl- acetamide	
296	N-Ethyl-N'-{3-fluoro-4-[6-methoxy-7-(piperidin-4-ylmethoxy)-quinolin-4-yloxy]-phenyl}-N-methyloxalamide	

46. A compound for modulating kinase activity of formula A-B-C, or a pharmaceutically acceptable salt, hydrate, or prodrug thereof, wherein, A is selected from:

-R ³	R8—N 0-2	R ⁸ N O 1-4
0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	N N 1-4	0-2 R ⁹ R ¹⁰ R ¹¹
R8—N 0-2	R8 N N R8 1-4	O R8 N 1-4

N R8	NR8 () ₀₋₂	O N N 1-4
R ⁸	0 N 1-4	N 1-4
N 1-4	R ³ 1 2-4	N N 1-4
S(O) ₀₋₂	O S(O) ₀₋₂	0 1-4

B is selected from:

2-0 A1 R3-0 N	R ⁵ N A ¹	S(O) ₀₋₂ R ³ -O N
R3-0 A1	$R^{3}-O$ A^{1}	$S(O)_{0-2}$ A^1

and, C is selected from:

wherein R^2 is selected from -H, halogen, trihalomethyl, -CN, -NH₂, -NO₂, -OR³, -NR³R³, -S(O)₀₋₂R³, -SO₂NR³R³, -CO₂R³, -C(O)NR³R³, -N(R³)SO₂R³, -N(R³)CO₂R³, -N(R³)CO₂R³, and optionally substituted lower alkyl;

q is 0 to 2;

each R³ is independently selected from –H, optionally substituted lower alkyl, optionally substituted aryl, optionally substituted arylalkyl, and optionally substituted heteroarylalkyl;

two R³, together with the nitrogen to which they are attached, form a four- to seven-membered heteroalicyclic, said four- to seven-membered heteroalicyclic optionally containing one additional heteroatom; when one said additional heteroatom is a nitrogen, then said nitrogen is optionally substituted with a group selected from -H, trihalomethyl, -SO₂R⁵, -SO₂NR⁵R⁵, -CO₂R⁵, -C(O)NR⁵R⁵, -C(O)R⁵, and optionally substituted lower alkyl;

each R^{35} is independently selected from -H, -C(=O)R³, -C(=O)OR³, -C(=O)SR³, -SO₂R³, -C(=O)N(R³)R³, and optionally substituted lower alkyl;

two R^{35} , together with the nitrogen to which they are attached, can combine to form a heteroalicyclic optionally substituted with between one and four of R^{60} , said heteroalicyclic may have an additional annular heteroatom, and said heteroalicyclic may have an aryl fused thereto, said aryl optionally substituted with an additional one to four of R^{60} ;

 A^1 is selected from =N-, =C(H)-, and =C(CN)-;

 A^2 is either =N- or =C(H)-;

R⁵ is -H or optionally substituted lower alkyl;

 R^8 is selected from R^3 , $-SO_2NR^3R^3$, $-CO_2R^3$, $-C(O)NR^3R^3$, $-SO_2R^3$, and $-C(O)R^3$;

R⁹, R¹⁰, and R¹¹ are each independently selected from -H, and -OR¹²; or

R⁹ is selected from -H, and -OR¹², and R¹⁰ and R¹¹, when taken together, are either an optionally substituted alkylidene or an oxo; and

R¹² is selected from -H, -C(O)R³, optionally substituted lower alkylidyne, optionally substituted lower arylalkylidyne, optionally substituted lower heterocyclylalkylidyne, optionally substituted lower alkylidene, optionally substituted lower alkylideneheterocyclyl, optionally substituted lower alkyl, optionally substituted lower alkylaryl, optionally substituted aryl, optionally substituted lower heterocyclylalkyl, and optionally substituted heterocyclyl;

or two R^{12} 's, when taken together, form 1) a corresponding spirocyclic ketal when said two R^{12} 's stem from R^{10} and R^{11} , or 2) a corresponding cyclic ketal when said two R^{12} 's stem from R^9 and one of R^{10} and R^{11} ;

 E^1 is selected from -O-, -CH₂-, -N(R⁵)-, and -S(O)₀₋₂-;

Q is a five- to ten-membered ring system, optionally substituted with between zero and four of R²⁰;

 R^{20} is selected from -H, halogen, trihalomethyl, -CN, -NO₂, -NH₂, -OR³, -NR³R³, -S(O)₀₋₂R³, -SO₂NR³R³, -CO₂R³, -C(O)NR³R³, -N(R³)SO₂R³, -N(R³)CO₂R³, -N(R³)CO₂R³, and optionally substituted lower alkyl;

 R^{60} is selected from -H, halogen, trihalomethyl, -CN, -NO₂, -NH₂, -OR³, -NR³R³, -S(O)₀₋₂R³, -SO₂NR³R³, -CO₂R³, -C(O)NR³R³, -N(R³)SO₂R³, -N(R³)C(O)R³,

 $-N(R^3)CO_2R^3$, $-C(O)R^3$, optionally substituted lower alkyl, optionally substituted aryl, optionally substituted heteroarylalkyl, and optionally substituted arylalkyl;

two of R⁶⁰, when attached to a non-aromatic carbon, can be oxo;

each methylene in any of the above formulae is independently optionally substituted with R^{25} :

each R^{25} is independently selected from halogen, trihalomethyl, -CN, -NO₂, -NH₂, -OR³, -NR³R³, -S(O)₀₋₂R³, -SO₂NR³R³, -CO₂R³, -C(O)NR³R³, -N(R³)SO₂R³, -N(R³)C(O)R³, -N(R³)CO₂R³, -C(O)R³, optionally substituted aryl, optionally substituted arylalkyl, heteroarylalkyl, and optionally substituted lower alkyl; two of R²⁵, together with the carbon or carbons to which they are attached, can combine to form a three- to seven-membered alicyclic or heteroalicyclic, two of R²⁵ on a single carbon can be oxo;

with the proviso that when B is selected from:

 A^2 (B^2)

and C contains $(R^2)_q$, and the remaining portion of C contains one of:

~ H ~ ~ ~		~ \
The second secon		∠ ^N →
\s\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\	~s~~>	0 - St- >St-
28/0	√N	<°>>>

directly attached to
$$(R^2)_q$$
 , then A must be one of:

N R8	R8—N 0-2	R ⁸ N O O O O O O O O O O O O O O O O O O
O O O O O O O O O O O O O O O O O O O	N N 1-4	0-2 R ⁹ R ¹⁰ R ¹¹
R8—N ()0-2	R ⁸ N N R ⁸ 1-4	O R8 N 1-4
N N N $1-4$	NR ⁸ () ₀₋₂	

and with the proviso that when C contains
$$(\mathsf{R}^2)_q$$
 , and B is selected from:

then the portion of C directly attached to

cannot contain

$$\mathbb{R}^{70}$$
 \mathbb{R}^{70} , when \mathbb{R}^{70} is selected from -H, $\mathbb{C}_{1\text{-4}}$ alkyl, and $\mathbb{C}_{1\text{-4}}$ alkoxyl.

- 47. The compound according to claim 46, wherein Q is selected from phenyl, napthyl, 1,2,3,4-tetrahydronaphthyl, indanyl, benzodioxanyl, benzofuranyl, phenazinyl, phenothiazinyl, phenoxazinyl, tetrahydroisoquinolyl, pyrrolyl, pyrazolyl, pyrazolidinyl, imidazolyl, imidazolinyl, imidazolidinyl, tetrahydropyridinyl, pyridinyl, pyrazinyl, pyrimidinyl, pyridazinyl, oxazolyl, oxazolinyl, oxazolidinyl, triazolyl, isoxazolyl, isoxazolidinyl, thiazolyl, thiazolinyl, thiazolidinyl, isothiazolyl, isothiazolidinyl, indolyl, isoindolyl, indolinyl, isoindolinyl, octahydroindolyl, octahydroisoindolyl, quinolyl, isoquinolyl, benzimidazolyl, thiadiazolyl, benzopyranyl, benzothiazolyl, benzoxazolyl, furyl, thienyl, benzothieliyl, and oxadiazolyl; each optionally substituted with between one and four of R²⁰; wherein each R²⁰ is independently selected from -H, halogen. trihalomethyl, -CN, -NO₂, -NH₂, -OR³, -NR³R³, -CO₂R³, -C(O)NR³R³, -N(R³)SO₂R³, $-N(R^3)C(O)R^3$, $-N(R^3)CO_2R^3$, $-C(O)R^3$, and optionally substituted lower alkyl.
- 48. The compound according to claim 47, wherein B is either of the following:

$$R^3-O$$
 A^1
 A^1
 A^1
 A^1
 A^1

wherein A^1 is either =N- or =C(H)-.

49. The compound according to claim 48, wherein B is

50. The compound according to claim 49, wherein C is selected from:

wherein R², R³, R⁵, R²⁰, R²⁵ and R⁶⁰ are as defined above.

- 51. The compound according to claim 50, R^2 is selected from halogen, trihalomethyl, -CN, -NO₂, -OR³, -NR³R³, -CO₂R³, -C(O)NR³R³, -N(R³)C(O)R³, -N(R³)CO₂R³, -C(O)R³, and optionally substituted lower alkyl
- 52. The compound according to claim 51, wherein R^2 is halogen.
- 53. The compound according to claim 52, wherein R² is either fluorine or chlorine.
- 54. A compound for modulating kinase activity according to Formula XI,

$$(R^{1})_{0-4} - (R^{2})_{0-4}$$

$$(R^{1})_{0-4} - (R^{2})_{0-4}$$

$$XI$$

or a pharmaceutically acceptable salt, hydrate, or prodrug thereof, wherein,

each R^1 is independently selected from halogen, -OR³, -NO₂, -NH₂, -NR³R⁴, -D-R⁵⁰ and optionally substituted C_{1-6} alkyl;

 R^{70} is selected from -H, halogen, -OR³, -S(O)₀₋₂R³, -NO₂, -NH₂, -NR³R⁴, and optionally substituted C₁₋₆alkyl;

Q is selected from =N-, =C(H)-, and =C(CN)-;

Z is selected from $-S(O)_{0-2}$, -O, and $-NR^5$ -;

Ar is either a five- or six-membered arylene or a five- or six-membered heteroarylene containing between one and three heteroatoms;

G is either an optionally substituted cycloalkyl or an optionally substituted heteroalicyclic; each R^2 is independently selected from halogen, trihalomethyl, -CN, -NO₂, -NH₂, -OR³, -NR³R⁴, -S(O)₀₋₂R³, -SO₂NR³R³, -CO₂R³, -C(O)NR³R³, -N(R³)SO₂R³, -N(R³)C(O)R³, -N(R³)CO₂R³, -C(O)R³, and optionally substituted C₁₋₆alkyl;

each R³ is independently -H or R⁴;

each R^4 is independently selected from optionally substituted $C_{1\text{-}6}$ alkyl, optionally substituted aryl, optionally substituted aryl $C_{1\text{-}6}$ alkyl, optionally substituted heterocyclyl, and optionally substituted heterocyclyl $C_{1\text{-}6}$ alkyl; or

R³ and R⁴, when taken together with a common nitrogen to which they are attached, form an optionally substituted five- to seven-membered heterocyclyl, said optionally substituted five- to seven-membered heterocyclyl optionally containing at least one additional annular heteroatom selected from N, O, S, and P;

 R^5 is -H or optionally substituted C_{1-6} alkyl;

each D is independently selected from -O-, -S(O) $_{0\text{-}2}$ -, and -NR 5 -;

each R^{50} is independently either R^3 , or according to formula XII;

$$(X^{1})_{m}$$
 $(X^{3})_{n}$
 $(X^{1})_{p}$

wherein X^1 , X^2 , and optionally X^3 , represent the atoms of a saturated bridged ring system, said saturated bridged ring system comprising up to four annular heteroatoms represented by any of X^1 , X^2 , and X^3 ; wherein,

each X^1 is independently selected from $-C(R^6)R^7$ -, -O-, $-S(O)_{0-2}$ -, and $-NR^8$ -;

each X^2 is independently an optionally substituted bridgehead methine or a bridgehead nitrogen;

each X^3 is independently selected from $-C(R^6)R^7$ -, -O-, $-S(O)_{0-2}$ -, and $-NR^8$ -;

Y is either:

an optionally substituted lower alkylene linker, between D and either 1) any annular atom of the saturated bridged ring system, except X^2 when X^2 is a bridgehead nitrogen, or 2) any heteroatom, represented by any of R^6 or R^7 ; provided there are at least two carbon atoms between D and any annular heteroatom of the saturated bridged ring system or any heteroatom represented by any of R^6 or R^7 ;

or Y is absent, when Y is absent, said saturated bridged ring system, is directly attached to D via an annular carbon of said saturated bridged ring system, unless D is -SO₂-, in which case said saturated bridged ring system, is directly attached to D via an any annular atom of said saturated bridged ring system;

m and p are each independently one to four;

n is zero to two, when n equals zero, then there is a single bond between the two bridgehead X^2 's;

 R^6 and R^7 are each independently selected from -H, halogen, trihalomethyl, -CN, -NH₂, -NO₂, -OR³, -NR³R⁴, -S(O)₀₋₂R⁴, -SO₂NR³R⁴, -CO₂R³, -C(O)NR³R⁴, -N(R³)SO₂R⁴, -N(R³)C(O)R³, -NCO₂R³, -C(O)R³, optionally substituted C₁₋₆alkyl, optionally substituted aryl, optionally substituted heterocyclyl C₁₋₆alkyl, and a bond to either Y or D; or

 R^6 and R^7 , when taken together are oxo; or

R⁶ and R⁷, when taken together with a common carbon to which they are attached, form a optionally substituted three- to seven-membered spirocyclyl, said optionally substituted three- to seven-membered spirocyclyl optionally containing at least one additional annular heteroatom selected from N, O, S, and P;

 R^8 is selected from $-R^3$, Y, $-SO_2NR^3R^4$, $-CO_2R^4$, $-C(O)NR^3R^3$, $-SO_2R^4$, and $-C(O)R^3$; and each R^{30} is independently selected from halogen, trihalomethyl, -CN, $-NO_2$, $-NH_2$, $-OR^3$, $-NR^3R^4$, $-S(O)_{0-2}R^3$, $-SO_2NR^3R^3$, $-CO_2R^3$, $-C(O)NR^3R^3$, $-N(R^3)SO_2R^3$, $-N(R^3)C(O)R^3$, $-N(R^3)CO_2R^3$, $-C(O)R^3$, and optionally substituted C_{1-6} alkyl.

- 55. The compound according to claim 54, wherein Z is either -O- or -NR⁵-.
- 56. The compound according to claim 55, wherein at least one of R^1 is -D- R^{50} .

57. The compound according to claim 56, wherein D is -O- and at least one other R¹ is -OR³.

58. The compound according to claim 57, of formula XIIIa or XIIIb:

wherein Q^1 is either =N- or =C(H)-.

- 59. The compound according to claim 58, wherein R^{50} is selected from C_{1-6} alkyl optionally substituted with at least one of optionally substituted amino, optionally substituted C_{1-6} alkyl amino, optionally substituted C_{1-6} dialkyl amino, optionally substituted heteroalicylic, and a group of formula **XII**.
- 60. The compound according to claim 59, wherein R^{3a} is C_{1-6} alkyl.
- 61. The compound according to claim 60, wherein Z is -O-.
- 62. The compound according to claim 61, wherein G is selected from cyclopropyl, aziradine, cyclobutyl, and azetidine, each optionally substituted with between zero and four of \mathbb{R}^{30} .
- 63. The compound according to claim 62, wherein Q is either =N- or =C(H)-.
- 64. The compound according to claim 63, wherein R^2 is selected from -H, halogen, C_{1-6} alkyl and perfluoro C_{1-6} alkyl.
- 65. The compound according to claim 64, wherein $-N(R^{3b})R^4$ is selected from the following:

wherein J, is a five- to ten-membered ring, optionally substituted with between zero and five of R²⁰;

each R^{20} is independently selected from -H, halogen, trihalomethyl, -CN, -NO₂, -NH₂, -OR³, -NR³R⁴, -S(O)₀₋₂R³, -SO₂NR³R³, -CO₂R³, -C(O)NR³R³, -N(R³)SO₂R³, -N(R³)C(O)R³, -N(R³)CO₂R³, -C(O)R³, optionally substituted C_{1-6} alkyl, optionally substituted aryl, optionally substituted heterocyclyl, and optionally substituted heterocyclyl C_{1-6} alkyl;

two of R²⁰, together with the atom or atoms to which they are attached, combine to form an optionally substituted three- to seven-membered heteroalicyclic, said optionally substituted three- to seven-membered heteroalicyclic either spiro- to J or fused to J;

E is selected from -O-, -N(R^5)-, -CH₂-, and -S(O)₀₋₂-;

each R^{60} is independently selected from halogen, trihalomethyl, -CN, -NO₂, -NH₂, -OR³, -NR³R⁴, -S(O)₀₋₂R³, -SO₂NR³R³, -CO₂R³, -C(O)NR³R³, -N(R³)SO₂R³, -N(R³)C(O)R³, -N(R³)CO₂R³, -C(O)R³, optionally substituted C_{1-6} alkyl, optionally substituted aryl, optionally substituted heteroaryl C_{1-6} alkyl, and optionally substituted aryl C_{1-6} alkyl;

each methylene in any of the above formulae, other than those in a depicted ring, is independently optionally substituted with R^{25} ; and

 R^{25} is selected from halogen, trihalomethyl, oxo, -CN, -NO₂, -NH₂, -OR³, -NR³R⁴, -S(O)₀₋₂R³, -SO₂NR³R³, -CO₂R³, -C(O)NR³R³, -N(R³)SO₂R³, -N(R³)C(O)R³, -N(R³)CO₂R³, -C(O)R³, optionally substituted aryl, optionally substituted aryl C₁₋₆alkyl, heteroaryl C₁₋₆alkyl, and optionally substituted C₁₋₆alkyl; or

two of R²⁵, together with the carbon or carbons to which they are attached, can combine to form a three- to seven-membered alicyclic or heteroalicyclic;

R^{3b} is equivalent to R³ as defined above; and

R⁴ and R⁵ are as defined above.

66. The compound according to claim 65, of formula XIVa or XIVb:

- 67. The compound according to claim 66, wherein R^{50} is $C_{1\text{-}6}$ alkyl optionally substituted with a group selected from optionally substituted amino, an optionally substituted alkylamino, optionally substituted dialkylamino, and optionally substituted heteroalicylic.
- 68. The compound according to claim 67, wherein the heteroalicyclic portion of said optionally substituted heteroalicyclic of R⁵⁰ is selected from the group consisting of piperidine, piperazine, morpholine, thiomorpholine, thiomorpholine 1-oxide, thiomorpholine 1,1-dioxide, 2-oxo-morpholine, pyrrolidine, and azepine.
- 69. The compound according to claim 67, wherein R^{50} is according to formula XII.
- 70. The compound according to claim 69, wherein the saturated bridged ring system according to formula **XII** has a geometry selected from the group consisting of [4.4.0], [4.3.0], [4.2.0], [4.1.0], [3.3.0], [3.2.0], [3.1.0], [3.3.3], [3.3.2], [3.3.1], [3.2.2], [3.2.1], [2.2.2], and [2.2.1].
- 71. The compound according to claim 70, wherein Y is selected from $-CH_2CH_2CH_2CH_2-$, $-CH_2CH_2CH_2-$, $-CH_2CH_2-$, $-CH_2CH_2-$, and absent.

72. The compound according to claim 71, wherein n is 0 and the saturated bridged ring system according to formula **XII** has a geometry selected from the group consisting of [4.4.0], [4.3.0], [4.2.0], [4.1.0], [3.3.0], [3.2.0], and [3.1.0].

- 73. The compound according to claim 72, wherein said saturated bridged ring system contains at least one annular nitrogen or at least one annular oxygen.
- 74. The compound according to claim 73, wherein said saturated bridged ring system contains -NR⁸-, wherein R⁸ is selected from -H, optionally substituted C_{1-6} alkyl, -CO₂R³, -C(O)NR³R³, -SO₂R³, and -C(O)R³.
- 75. The compound according to claim 73, wherein said saturated bridged ring system is of formula XV,

XV

wherein U^1 is selected from -O-, -S(O)₀₋₂-, -NR⁸-, -CR⁶R⁷-, and absent; and e is 0 or 1.

- 76. The compound according to claim 75, wherein Y is -CH₂-.
- 77. The compound according to claim 76, wherein U^1 is -NR⁸-, wherein R⁸ is selected from -H, optionally substituted lower alkyl, -CO₂R³, -C(O)NR³R³, -SO₂R³, and -C(O)R³.
- 78. The compound according to claim 76, wherein U^1 is -O-.
- 79. The compound according to claim 76, wherein U^1 is absent.
- 80. The compound according to claim 71, wherein Y is selected from - CH_2CH_2 -, - CH_2 -, and absent.
- 81. The compound according to claim 80, wherein said saturated bridged ring system is of formula **XVI**,

XVI

wherein R⁹, R¹⁰, and R¹¹ are each independently selected from -H, and -OR¹²; or

R⁹ is selected from -H, and -OR¹², and R¹⁰ and R¹¹, when taken together, are either an optionally substituted alkylidene or an oxo;

R¹² is selected from -H, -C(O)R³, optionally substituted lower alkylidyne, optionally substituted lower arylalkylidyne, optionally substituted lower alkylidene, optionally substituted lower alkylidenearyl, optionally substituted lower alkylideneheterocyclyl, optionally substituted lower alkyl, optionally substituted lower alkylaryl, optionally substituted aryl, optionally substituted lower heterocyclylalkyl, and optionally substituted heterocyclyl;

or two R^{12} 's, when taken together, form 1) a corresponding spirocyclic ketal when said two R^{12} 's stem from R^{10} and R^{11} , or 2) a corresponding cyclic ketal when said two R^{12} 's stem from R^{9} and one of R^{10} and R^{11} .

- 82. The compound according to claim 81, wherein one of R^{10} and R^{11} is $-OR^{12}$, wherein R^{12} is selected from -H, -C(O) R^3 , and optionally substituted lower alkyl; and R^9 and the other of R^{10} and R^{11} are both -H.
- 83. The compound according to claim 82, wherein Y is either -CH₂- or absent.
- 84. The compound according to claim 81, wherein R⁹ is an alkyl group containing at least one fluorine substitution thereon.
- 85. The compound according to claim 74, wherein said saturated bridged ring system is of formula **XVII**.

XVII

86. The compound according to claim 85, wherein Y is either -CH₂- or absent.

- 87. The compound according to claim 86, wherein R⁸ is methyl or ethyl.
- 88. The compound according to claim 87, wherein at least one of R² is halogen.
- 89. The compound according to claim 74, wherein said saturated bridged ring system is of formula **XVIII**.

- 90. The compound according to claim 89, wherein Y is -CH₂-.
- 91. The compound according to claim 90, wherein R⁸ is methyl or ethyl.
- 92. The compound according to claim 73, wherein said saturated bridged ring system is of formula **XIX**

$$O \bigvee_{N}^{\mathbb{R}^3} \bigvee_{1}^{\mathbb{R}^3}$$

XIX

wherein U^2 is selected from -O-, -S(O)₀₋₂-, -NR⁸-, -CR⁶R⁷-, and absent.

- 93. The compound according to claim 92, wherein R³ of formula **XIX** is selected from -H and optionally substituted alkyl.
- 94. The compound according to claim 93, wherein U^2 is either $-CR^6R^7$ or absent.
- 95. The compound according to claim 94, wherein U^2 is either -CH₂- or absent.
- 96. The compound according to claim 95, wherein Y is -CH₂-.
- 97. The compound according to claim 74, wherein said saturated bridged ring system is according to formula **XX**.

$\mathbf{X}\mathbf{X}$

- 98. The compound according to claim 97, wherein R⁸ is methyl or ethyl.
- 99. The compound according to any of claims 67 through 98, wherein R^2 is selected from C_{1-6} alkyl, perfluoro C_{1-6} alkyl, and halogen.
- 100. The compound according to claim 99, wherein R^2 is selected from perfluoro C_{1-3} alkyl and halogen.
- 101. The compound according to any of claims 67 through 98, wherein R^{20} is selected from halogen, -CN, -NO₂, -NH₂, -OR³, -NR³R⁴, -N(R³)SO₂R³, -N(R³)C(O)R³, -N(R³)CO₂R³, optionally substituted heterocyclyl, and optionally substituted heterocyclyl C₁₋₆alkyl, and (two of R²⁰) together with the atom or atoms to which they are attached, an optionally substituted three- to six-membered heteroalicyclic, said optionally substituted three- to six-membered heteroalicyclic fused to the phenyl as in **XIVa** or **XIVb**.
- 102. The compound according to claim 101, wherein R^{20} is selected from halogen, $-NR^3R^4$, optionally substituted heterocyclyl, and optionally substituted heterocyclyl C_{1-6} alkyl, and (two of R^{20}) together with the atom or atoms to which they are attached, an optionally substituted five- to six-membered heteroalicyclic, said optionally substituted five- to six-membered heteroalicyclic fused to the phenyl as in **XIVa** or **XIVb**.
- 103. The compound according to claim 102, wherein R^2 is selected from C_{1-6} alkyl, perfluoro C_{1-6} alkyl, and halogen.
- 104. The compound according to claim 103, wherein R^2 is selected from perfluoro C_{1-3} alkyl and halogen.
- 105. The compound according to claim 54, selected from Table 2.

Table 2

Entry	Name	Structure
1	N-(6-{[6,7-bis(methyloxy)quinolin-4-yl]oxy}-5-chloropyridin-3-yl)-N'-(4-fluorophenyl)cyclopropane-1,1-dicarboxamide	CI N N N N N N N N N N N N N N N N N N N
2	N-(6-{[6,7-bis(methyloxy)quinolin-4-yl]oxy}-5-chloropyridin-3-yl)-N'-(4-fluorophenyl)cyclobutane-1,1-dicarboxamide	CI N N O O F
3	N-(6-{[6,7-bis(methyloxy)quinolin-4-yl]oxy}-5-chloropyridin-3-yl)-N'- (phenylmethyl)cyclopropane-1,1-dicarboxamide	CITAL
4	N-(6-{[6,7-bis(methyloxy)quinolin-4-yl]oxy}-5-chloropyridin-3-yl)-N'-phenylcyclopropane-1,1-dicarboxamide	CI N H T H
5	N-[3-fluoro-4-({6- (methyloxy)-7-[(3- morpholin-4- ylpropyl)oxy]quinolin-4- yl}oxy)phenyl]-N'-(4- fluorophenyl)cyclopropan e-1,1-dicarboxamide	
6	N-[3-fluoro-4-({6- (methyloxy)-7-[(3- piperidin-1- ylpropyl)oxy]quinolin-4- yl}oxy)phenyl]-N'-(4- fluorophenyl)cyclopropan e-1,1-dicarboxamide	F H T H T F

Table 2

Entry	Name	Structure
7	N-[3-fluoro-4-({6- (methyloxy)-7-[(3- piperidin-1- ylpropyl)oxy]quinolin-4- yl}oxy)phenyl]-N'-(4- fluorophenyl)cyclobutane -1,1-dicarboxamide	F H H H H H H H H H H H H H H H H H H H
8	N-(6-{[6,7-bis(methyloxy)quinolin-4-yl]oxy}-5-chloropyridin-3-yl)-N'-(2-phenylethyl)cyclopropane-1,1-dicarboxamide	CI N N N N N N N N N N N N N N N N N N N
9	N-(6-{[6,7-bis(methyloxy)quinolin-4-yl]oxy}-2-methylpyridin-3-yl)-N'-(4-fluorophenyl)cyclopropane-1,1-dicarboxamide	H H H H H H H H H H H H H H H H H H H
10	N-{4-[(7-chloroquinolin- 4-yl)oxy]-3- fluorophenyl}-N'-(4- fluorophenyl)cyclopropan e-1,1-dicarboxamide	F H F
11	N-{4-[(7-chloroquinolin- 4-yl)oxy]phenyl}-N'-(4- fluorophenyl)cyclopropan e-1,1-dicarboxamide	CI
12	N-(4-{[6,7-bis(methyloxy)quinolin-4-yl]oxy}phenyl)-N'-(4-fluorophenyl)cyclopropane-1,1-dicarboxamide	

Table 2

· · · · · · · · · · · · · · · · · · ·	Table 2		
Entry	Name	Structure	
13	N-(4-{[6,7-bis(methyloxy)quinazolin -4-yl]oxy}phenyl)-N'-(4-fluorophenyl)cyclopropan e-1,1-dicarboxamide	O THE STATE OF THE	
14	N-(4-{[6,7-bis(methyloxy)quinazolin -4-yl]oxy}-3-fluorophenyl)-N'-(4-fluorophenyl)cyclopropan e-1,1-dicarboxamide	F N N F	
15	N-[3-fluoro-4-({6- (methyloxy)-7-[(3- morpholin-4- ylpropyl)oxy]quinazolin- 4-yl}oxy)phenyl]-N'-(4- fluorophenyl)cyclopropan e-1,1-dicarboxamide	F H N F	
16	N-{5-chloro-6-[(6- (methyloxy)-7-{[(1- methylpiperidin-4- yl)methyl]oxy}quinolin- 4-yl)oxy]pyridin-3-yl}- N'-(4- fluorophenyl)cyclopropan e-1,1-dicarboxamide	CI N H N F	
17	N-[5-chloro-6-({6- (methyloxy)-7- [(piperidin-4- ylmethyl)oxy]quinolin-4- yl}oxy)pyridin-3-yl]-N'- (4- fluorophenyl)cyclopropan e-1,1-dicarboxamide	CI HIN HIN HIN HIN HIN HIN HIN HIN HIN HI	
18	N-[5-chloro-6-({6- (methyloxy)-7- [(phenylmethyl)oxy]quino lin-4-yl}oxy)pyridin-3- yl]-N'-(4- fluorophenyl)cyclopropan e-1,1-dicarboxamide	CI THE THE PERSON OF THE PERSO	

Table 2

Entry	Name	Structure
19	N-(4-{[7-{[2- (diethylamino)ethyl]oxy}- 6-(methyloxy)quinolin-4- yl]oxy}-3-fluorophenyl)- N'-(4- fluorophenyl)cyclopropan e-1,1-dicarboxamide	F T T T T T T T T T T T T T T T T T T T
20	N-(4-{[7-{[2- (diethylamino)ethyl]oxy}- 6-(methyloxy)quinolin-4- yl]oxy}-3-fluorophenyl)- N'-(4- fluorophenyl)cyclobutane -1,1-dicarboxamide	F N N N N N N N N N N N N N N N N N N N
21	N-{3-fluoro-4-[(6- (methyloxy)-7-{[(1- methylpiperidin-4- yl)methyl]oxy}quinazolin -4-yl)oxy]phenyl}-N'-(4- fluorophenyl)cyclopropan e-1,1-dicarboxamide	F N N N F
22	N-(4-{[6,7-bis(methyloxy)quinolin-4-yl]oxy}-2-methylphenyl)-N'-(4-fluorophenyl)cyclopropane-1,1-dicarboxamide	
23	N-(4-fluorophenyl)-N'-[2-methyl-6-({6- (methyloxy)-7-[(3- morpholin-4- ylpropyl)oxy]quinolin-4- yl}oxy)pyridin-3- yl]cyclopropane-1,1- dicarboxamide	
24	N-(4-{[6,7-bis(methyloxy)quinolin-4-yl]oxy}-3-fluorophenyl)-N'-(4-fluorophenyl)cyclopropane-1,1-dicarboxamide	F H T H T H T H T H T H T H T H T H T H

Table 2

Entry	Name	Structure
25	N-(6-{[6,7-bis(methyloxy)quinolin-4-yl]oxy}-5-chloro-2-methylpyridin-3-yl)-N'-(4-fluorophenyl)cyclopropane-1,1-dicarboxamide	CI THE THE F
26	N-[3-fluoro-4-({7- (methyloxy)-6-[(3- morpholin-4- ylpropyl)oxy]quinazolin- 4-yl}oxy)phenyl]-N'-(4- fluorophenyl)cyclopropan e-1,1-dicarboxamide	F N N N F
27	N-(4-{[6,7-bis(methyloxy)quinolin-4-yl]oxy}-3,5-difluorophenyl)-N'-(4-fluorophenyl)cyclopropane-1,1-dicarboxamide	F H H H H H H H H H H H H H H H H H H H
28	N-(4-{[6,7-bis(methyloxy)quinolin-4-yl]oxy}-2,5-difluorophenyl)-N'-(4-fluorophenyl)cyclopropane-1,1-dicarboxamide	F N N F
29	N-[3-fluoro-4-({7- (methyloxy)-6-[(3- morpholin-4- ylpropyl)oxy]quinolin-4- yl}oxy)phenyl]-N'-(4- fluorophenyl)cyclopropan e-1,1-dicarboxamide	F H T H T F
30	N-{3-fluoro-4-[(6- (methyloxy)-7-(2-methyl octahydrocyclo- penta[c]pyrrol-5- ylmethoxy)quinazolin-4- yl)oxy]phenyl}-N'-(4- fluorophenyl)cyclopropan e-1,1-dicarboxamide	F H T H T F

Table 2

Entry	Name	Structure
31	N-{3-fluoro-4-[(7- (methyloxy)-6-{[(1- methylpiperidin-4- yl)methyl]oxy}quinazolin -4-yl)oxy]phenyl}-N'-(4- fluorophenyl)cyclopropan e-1,1-dicarboxamide	F H T H T F
32	N-[5-fluoro-2-methyl-4- ({6-(methyloxy)-7-[(3- morpholin-4- ylpropyl)oxy]quinolin-4- yl}oxy)phenyl]-N'-(4- fluorophenyl)cyclopropan e-1,1-dicarboxamide	
33	N-(4-{[6,7-bis(methyloxy)quinolin-4-yl]oxy}-2,3,5-trifluorophenyl)-N'-(4-fluorophenyl)cyclopropane-1,1-dicarboxamide	F H N H N F
34	N-(4-{[6,7-bis(methyloxy)quinolin-4-yl]oxy}-5-fluoro-2-methylphenyl)-N'-(4-fluorophenyl)cyclopropane-1,1-dicarboxamide	F H T H T H T H T H T H T H T H T H T H
35	N-(4-{[6,7-bis(methyloxy)quinolin-4-yl]oxy}-2-chloro-5-methylphenyl)-N'-(4-fluorophenyl)cyclopropane-1,1-dicarboxamide	H CI OF F
36	N-(3-fluoro-4-{[6- hydroxy-7- (methyloxy)quinolin-4- yl]oxy}phenyl)-N'-(4- fluorophenyl)cyclopropan e-1,1-dicarboxamide	F HO F

Table 2

Entry	Name	Structure
37	N-(4-fluorophenyl)-N'-[2-methyl-4-({6-(methyloxy)-7-[(3-morpholin-4-ylpropyl)oxy]quinolin-4-yl}oxy)phenyl]cyclopropane-1,1-dicarboxamide	
38	N-[3-fluoro-4-({6- (methyloxy)-7-[(3- piperazin-1- ylpropyl)oxy]quinolin-4- yl}oxy)phenyl]-N'-(4- fluorophenyl)cyclopropan e-1,1-dicarboxamide	
39	N-{3-fluoro-4-[(6- (methyloxy)-7-{[3-(4- methylpiperazin-1- yl)propyl]oxy}quinolin-4- yl)oxy]phenyl}-N'-(4- fluorophenyl)cyclopropan e-1,1-dicarboxamide	F N N N N N N N N N N N N N N N N N N N
40	N-{3-fluoro-4-[(6- (methyloxy)-7-{[(1- methylpiperidin-4- yl)methyl]oxy}quinolin- 4-yl)oxy]phenyl}-N'-(4- fluorophenyl)cyclopropan e-1,1-dicarboxamide	HN NH N

Table 2

Entry	Name	Structure
41	N-(4-fluorophenyl)-N'-[4- ({6-(methyloxy)-7-[(3- morpholin-4- ylpropyl)oxy]quinolin-4- yl}oxy)phenyl]cyclopropa ne-1,1-dicarboxamide	F NH O NH
42	N-(4-{[7-{[3- (diethylamino)propyl]oxy }-6-(methyloxy)quinolin- 4-yl]oxy}-3- fluorophenyl)-N'-(4- fluorophenyl)cyclopropan e-1,1-dicarboxamide	F NH
43	N-(4-{[6,7-bis(methyloxy)quinolin-4-yl]oxy}-2-chloro-5-fluorophenyl)-N'-(4-fluorophenyl)cyclopropane-1,1-dicarboxamide	F O OCI O N N N N N N N N N N N N N N N N N N
44	N-(4-{[6,7-bis(methyloxy)-2-(methylthio)quinolin-4-yl]oxy}-3-fluorophenyl)-N'-(4-fluorophenyl)cyclopropane-1,1-dicarboxamide	F N N N N N N N N N N N N N N N N N N N
45	N-(4-fluorophenyl)-N'-(4- {[2-methyl-6,7- bis(methyloxy)quinazolin -4- yl]oxy}phenyl)cyclopropa ne-1,1-dicarboxamide	F N N N N

Table 2

Entry	Name	Structure
46	N-(4-{[2-amino-6,7-bis(methyloxy)quinolin-4-yl]oxy}-3-fluorophenyl)-N'-(4-fluorophenyl)cyclopropane-1,1-dicarboxamide	F N N N N N N N N N N N N N N N N N N N
47	N-(3-fluoro-4-{[2- (methylamino)-6,7- bis(methyloxy)quinolin-4- yl]oxy}phenyl)-N'-(4- fluorophenyl)cyclopropan e-1,1-dicarboxamide	H H H H H H H H H H H H H H H H H H H
48	(1S,2R)-N-[3-fluoro-4- ({6-(methyloxy)-7-[(3- morpholin-4- ylpropyl)oxy]quinolin-4- yl}oxy)phenyl]-N'-(4- fluorophenyl)-2- methylcyclopropane-1,1- dicarboxamide	HN OHN OHN OHN OHN OHN OHN OHN OHN OHN O
49	(1R,2R)-N-[3-fluoro-4- ({6-(methyloxy)-7-[(3- morpholin-4- ylpropyl)oxy]quinolin-4- yl}oxy)phenyl]-N'-(4- fluorophenyl)-2- methylcyclopropane-1,1- dicarboxamide	

Table 2

Entry	Name	Structure
50	N-(4-{[6-{[3- (diethylamino)propyl]oxy }-7-(methyloxy)quinolin- 4-yl]oxy}-3- fluorophenyl)-N'-(4- fluorophenyl)cyclopropan e-1,1-dicarboxamide	HN O F O
51	N-(4-{[6-{[2- (diethylamino)ethyl]oxy}- 7-(methyloxy)quinolin-4- yl]oxy}-3-fluorophenyl)- N'-(4- fluorophenyl)cyclopropan e-1,1-dicarboxamide	HN F O
52	1,1-dimethylethyl 4-(3- {[4-[(2-fluoro-4-{[(1- {[(4- fluorophenyl)amino]carbo nyl}cyclopropyl)carbonyl]amino}phenyl)oxy]-6- (methyloxy)quinolin-7- yl]oxy}propyl)piperazine- 1-carboxylate	O N N N N N N N N N N N N N N N N N N N
53	(1R,2R)-N-[3-fluoro-4- ({6-(methyloxy)-7-[(3- morpholin-4- ylpropyl)oxy]quinazolin- 4-yl}oxy)phenyl]-N'-(4- fluorophenyl)-2- methylcyclopropane-1,1- dicarboxamide	P P P P P P P P P P P P P P P P P P P

Table 2

TC4	Norma	Structure
Entry	Name	Structure
54	(1R,2R)-N-(4-{[7-{[2- (diethylamino)ethyl]oxy}- 6-(methyloxy)quinazolin- 4-yl]oxy}-3- fluorophenyl)-N'-(4- fluorophenyl)-2- methylcyclopropane-1,1- dicarboxamide	F O HN O H
55	N-(4-{[7-{[3- (diethylamino)propyl]oxy }-6- (methyloxy)quinazolin-4- yl]oxy}-3-fluorophenyl)- N'-(4- fluorophenyl)cyclopropan e-1,1-dicarboxamide	F N N N N
56	N-(4-{[7-{[3-(4-acetylpiperazin-1-yl)propyl]oxy}-6-(methyloxy)quinolin-4-yl]oxy}-3-fluorophenyl)-N'-(4-fluorophenyl)cyclopropane-1,1-dicarboxamide	F O N N N N N N N N N N N N N N N N N N
57	1,1-dimethylethyl 4-(3- {[4-[(2-fluoro-4- {[((1R,2R)-1-{[(4- fluorophenyl)amino]carbo nyl}-2- methylcyclopropyl)carbon yl]amino}phenyl)oxy]-6- (methyloxy)quinolin-7- yl]oxy}propyl)piperazine- 1-carboxylate	F HZ F

Table 2

Entry	Name	Structure
58	N-(4-{[6,7-bis(methyloxy)quinolin-4-yl]oxy}phenyl)-N'-(4-fluorophenyl)-1-(phenylmethyl)azetidine-3,3-dicarboxamide	NH O
59	N-(4-{[6,7-bis(methyloxy)quinolin-4-yl]oxy}phenyl)-N'-(4-fluorophenyl)azetidine-3,3-dicarboxamide	NH ONH HN HN
60	(1R,2S)-N-{3-fluoro-4- [(6-(methyloxy)-7-{[3-(4- methylpiperazin-1- yl)propyl]oxy}quinolin-4- yl)oxy]phenyl}-N'-(4- fluorophenyl)-2- methylcyclopropane-1,1- dicarboxamide	N HN O HN
61	(1R,2R)-N-{3-fluoro-4- [(6-(methyloxy)-7-{[3-(4- methylpiperazin-1- yl)propyl]oxy}quinolin-4- yl)oxy]phenyl}-N'-(4- fluorophenyl)-2- methylcyclopropane-1,1- dicarboxamide	N N F N N N N N N N N N N N N N N N N N

Table 2

Entry	Name	Structure
62	(1R,2R)-N-[3-fluoro-4- ({6-(methyloxy)-7-[(3- piperazin-1- ylpropyl)oxy]quinolin-4- yl}oxy)phenyl]-N'-(4- fluorophenyl)-2- methylcyclopropane-1,1- dicarboxamide	NH N N N N N N N N N N N N N N N N N N
63	N-(3-fluoro-4-{[7-({3-[4-(1-methylethyl)piperazin-1-yl]propyl}oxy)-6-(methyloxy)quinolin-4-yl]oxy}phenyl)-N'-(4-fluorophenyl)cyclopropane-1,1-dicarboxamide	E NH O NH
64	N-(4-{[7-{[3- (diethylamino)propyl]oxy }-6- (methyloxy)quinazolin-4- yl]oxy}-3-fluorophenyl)- N'-(4- fluorophenyl)cyclopropan e-1,1-dicarboxamide	F NH O N N N N
65	(1R,2R)-N-(4-{[7-{[3- (diethylamino)propyl]oxy }-6-(methyloxy)quinolin- 4-yl]oxy}-3- fluorophenyl)-N'-(4- fluorophenyl)-2- methylcyclopropane-1,1- dicarboxamide	F N O HN O

Table 2

Entry	Name	Structure
Enu y	1 value	Suucture
66	(1R,2R)-N-(4-{[7-{[2- (diethylamino)ethyl]oxy}- 6-(methyloxy)quinolin-4- yl]oxy}-3-fluorophenyl)- N'-(4-fluorophenyl)-2- methylcyclopropane-1,1- dicarboxamide	F N N N N N N N N N N N N N N N N N N N
67	(1R,2S)-N-(4-{[7-{[3- (diethylamino)propyl]oxy }-6-(methyloxy)quinolin- 4-yl]oxy}-3- fluorophenyl)-N'-(4- fluorophenyl)-2- methylcyclopropane-1,1- dicarboxamide	F N HN O
68	(1R,2S)-N-(4-{[7-{[2- (diethylamino)ethyl]oxy}- 6-(methyloxy)quinolin-4- yl]oxy}-3-fluorophenyl)- N'-(4-fluorophenyl)-2- methylcyclopropane-1,1- dicarboxamide	F N N N N N N N N N N N N N N N N N N N
69	N-(4-{[7-{[2- (diethylamino)ethyl]oxy}- 6-(methyloxy)quinazolin- 4-yl]oxy}-3- fluorophenyl)-N'-(4- fluorophenyl)cyclobutane -1,1-dicarboxamide	N N N N N N N N N N N N N N N N N N N

Table 2

Entry	Name	Structure
70	(1R,2S)-N-[3-fluoro-4- ({6-(methyloxy)-7-[(3- piperazin-1- ylpropyl)oxy]quinolin-4- yl}oxy)phenyl]-N'-(4- fluorophenyl)-2- methylcyclopropane-1,1- dicarboxamide	NH N N N N N N N N N N
71	(1R,2R,3S)-N-[3-fluoro- 4-({6-(methyloxy)-7-[(3- morpholin-4- ylpropyl)oxy]quinolin-4- yl}oxy)phenyl]-N'-(4- fluorophenyl)-2,3- dimethylcyclopropane- 1,1-dicarboxamide	F N HN O
72	(1R,2R,3S)-N-{3-fluoro-4-[(6-(methyloxy)-7-{[3-(4-methylpiperazin-1-yl)propyl]oxy}quinolin-4-yl)oxy]phenyl}-N'-(4-fluorophenyl)-2,3-dimethylcyclopropane-1,1-dicarboxamide	N N N N N N N N N N N N N N N N N N N
73	(1R,2R,3S)-N-[3-fluoro- 4-({6-(methyloxy)-7-[(3- morpholin-4- ylpropyl)oxy]quinazolin- 4-yl}oxy)phenyl]-N'-(4- fluorophenyl)-2,3- dimethylcyclopropane- 1,1-dicarboxamide	F O HIN O HI

Table 2

Entry	Name	Structure
74	(1R,2R,3S)-N-{3-fluoro-4-[(6-(methyloxy)-7-{[3-(4-methylpiperazin-1-yl)propyl]oxy}quinazolin-4-yl)oxy]phenyl}-N'-(4-fluorophenyl)-2,3-dimethylcyclopropane-1,1-dicarboxamide	F NH
75	N-[3-fluoro-4-({6- (methyloxy)-7-[(3- morpholin-4- ylpropyl)oxy]quinazolin- 4-yl}oxy)phenyl]-N'-(4- fluorophenyl)cyclobutane -1,1-dicarboxamide	
76	(2R,3R)-N-[3-fluoro-4- ({6-(methyloxy)-7-[(3- morpholin-4- ylpropyl)oxy]quinolin-4- yl}oxy)phenyl]-N'-(4- fluorophenyl)-2,3- dimethylcyclopropane- 1,1-dicarboxamide	
77	(2R,3R)-N-(4-{[7-{[3-(diethylamino)propyl]oxy}}-6-(methyloxy)quinolin-4-yl]oxy}-3-fluorophenyl)-N'-(4-fluorophenyl)-2,3-dimethylcyclopropane-1,1-dicarboxamide	F N O HN O HN O N N T N N N N N N N N N N N N N N N

Table 2

Entry	Name	Structure
78	N-(4-{[7-{[3- (diethylamino)propyl]oxy }-6-(methyloxy)quinolin- 4-yl]oxy}-3- fluorophenyl)-N'-(4- fluorophenyl)-2,2- dimethylcyclopropane- 1,1-dicarboxamide	P O HN O HN O
79	N-[3-fluoro-4-({6- (methyloxy)-7-[(3- morpholin-4- ylpropyl)oxy]quinazolin- 4-yl}oxy)phenyl]-N'-(4- fluorophenyl)-2,2- dimethylcyclopropane- 1,1-dicarboxamide	O HN O HN O O HN O O O O O O O O O O O O
80	(1R,2R,3S)-N-(4-{[7-{[3-(diethylamino)propyl]oxy}}-6-(methyloxy)quinolin-4-yl]oxy}-3-fluorophenyl)-N'-(4-fluorophenyl)-2,3-dimethylcyclopropane-1,1-dicarboxamide	P O HN O H
81	N-(4-{[7-{[2- (diethylamino)ethyl]oxy}- 6-(methyloxy)quinolin-4- yl]oxy}-3-fluorophenyl)- N'-(4-fluorophenyl)-2,2- dimethylcyclopropane- 1,1-dicarboxamide	F O HN O HN O
82	(1R,2R,3S)-N-(4-{[7-{[2-(diethylamino)ethyl]oxy}-6-(methyloxy)quinolin-4-yl]oxy}-3-fluorophenyl)-N'-(4-fluorophenyl)-2,3-dimethylcyclopropane-1,1-dicarboxamide	F O HN O HN O

Table 2

Entry	Name	Structure
83	N-[3-fluoro-4-({6- (methyloxy)-7-[(3- morpholin-4- ylpropyl)oxy]quinolin-4- yl}oxy)phenyl]-N'-(4- fluorophenyl)-2,2- dimethylcyclopropane- 1,1-dicarboxamide	P O HIN O HIN O
84	N-(4-{[7-{[2- (diethylamino)ethyl]oxy}- 6-(methyloxy)quinazolin- 4-yl]oxy}-3- fluorophenyl)-N'-(4- fluorophenyl)-2,2- dimethylcyclopropane- 1,1-dicarboxamide	N N F N N F
85	N-(4-{[7-{[3- (diethylamino)propyl]oxy }-6- (methyloxy)quinazolin-4- yl]oxy}-3-fluorophenyl)- N'-(4-fluorophenyl)-2,2- dimethylcyclopropane- 1,1-dicarboxamide	P O HN O HN O
86	N-(4-{[7-{[3- (diethylamino)propyl]oxy }-6- (methyloxy)quinazolin-4- yl]oxy}-3-fluorophenyl)- N'-(4- fluorophenyl)cyclobutane -1,1-dicarboxamide	N N N N N N N N N N N N N N N N N N N
87	N-{3-fluoro-4-[(6- (methyloxy)-7-{[3-(4- methylpiperazin-1- yl)propyl]oxy}quinazolin- 4-yl)oxy]phenyl}-N'-(4- fluorophenyl)cyclobutane -1,1-dicarboxamide	N N N N N N N N N N N N N N N N N N N

Table 2

Entry	Name	Structure
88	N-[3-fluoro-4-({6- (methyloxy)-7-[(3- piperazin-1- ylpropyl)oxy]quinazolin- 4-yl}oxy)phenyl]-N'-(4- fluorophenyl)cyclobutane -1,1-dicarboxamide	N-N-N-N-N-N-N-N-N-N-N-N-N-N-N-N-N-N-N-
89	(2R,3R)-N-[3-fluoro-4- ({6-(methyloxy)-7-[(3- morpholin-4- ylpropyl)oxy]quinazolin- 4-yl}oxy)phenyl]-N'-(4- fluorophenyl)-2,3- dimethylcyclopropane- 1,1-dicarboxamide	F O HIN O HI
90	N-(4-{[7-{[3- (diethylamino)propyl]oxy }-6-(methyloxy)quinolin- 4-yl]oxy}-3- fluorophenyl)-N'-(4- fluorophenyl)cyclobutane -1,1-dicarboxamide	N-N-NH NH NH
91	N-{3-fluoro-4-[(6- (methyloxy)-7-{[3-(4- methylpiperazin-1- yl)propyl]oxy}quinolin-4- yl)oxy]phenyl}-N'-(4- fluorophenyl)cyclobutane -1,1-dicarboxamide	N N N N N N N N N N N N N N N N N N N

Table 2

Entry	Name	Structure
92	(1R,2R)-N-(4-{[7-{[3- (diethylamino)propyl]oxy }-6- (methyloxy)quinazolin-4- yl]oxy}-3-fluorophenyl)- N'-(4-fluorophenyl)-2- methylcyclopropane-1,1- dicarboxamide	P O HN O H
93	(1R,2R)-N-{3-fluoro-4- [(6-(methyloxy)-7-{[3-(4- methylpiperazin-1- yl)propyl]oxy}quinazolin- 4-yl)oxy]phenyl}-N'-(4- fluorophenyl)-2- methylcyclopropane-1,1- dicarboxamide	N N F N N N N N N N N N N N N N N N N N
94	(2R,3R)-N-(4-{[7-{[2- (diethylamino)ethyl]oxy}- 6-(methyloxy)quinazolin- 4-yl]oxy}-3- fluorophenyl)-N'-(4- fluorophenyl)-2,3- dimethylcyclopropane- 1,1-dicarboxamide	N P N P N N P N N N P N N N P N N N P N N N N P N
95	(2R,3R)-N-(4-{[7-{[3- (diethylamino)propyl]oxy }-6- (methyloxy)quinazolin-4- yl]oxy}-3-fluorophenyl)- N'-(4-fluorophenyl)-2,3- dimethylcyclopropane- 1,1-dicarboxamide	F N N F N N F
96	(1R,2R)-N-[3-fluoro-4- ({6-(methyloxy)-7-[(3- piperazin-1- ylpropyl)oxy]quinazolin- 4-yl}oxy)phenyl]-N'-(4- fluorophenyl)-2- methylcyclopropane-1,1- dicarboxamide	N N F N N N N N N N N N N N N N N N N N

Table 2

Entry	Name	Structure
97	(2R,3R)-N-(4-{[7-{[2- (diethylamino)ethyl]oxy}- 6-(methyloxy)quinolin-4- yl]oxy}-3-fluorophenyl)- N'-(4-fluorophenyl)-2,3- dimethylcyclopropane- 1,1-dicarboxamide	N P N P N N N N N N N N N N N N N N N N
98	N-(4-{[6,7-bis(methyloxy)quinolin-4-yl]oxy}phenyl)-N'-[(4-fluorophenyl)methyl]cyclopropane-1,1-dicarboxamide	The state of the s
99	N-(4-{[6,7-bis(methyloxy)quinolin-4-yl]oxy}phenyl)-N'-(2-morpholin-4-ylethyl)cyclopropane-1,1-dicarboxamide	H N N N N N N N N N N N N N N N N N N N
100	N-(4-{[6,7-bis(methyloxy)quinolin-4-yl]oxy}phenyl)-N'-[2-(piperidin-1-ylmethyl)phenyl]cyclopropane-1,1-dicarboxamide	NH O NH O NN
101	N-(4-{[6,7-bis(methyloxy)quinolin-4-yl]oxy}phenyl)-N'-[2-(pyrrolidin-1-ylmethyl)phenyl]cyclopropane-1,1-dicarboxamide	NH O NN N

Table 2

Entry	Name	Structure
102	N-(4-{[6,7-bis(methyloxy)quinolin-4-yl]oxy}phenyl)-N'-[3-(morpholin-4-ylmethyl)phenyl]cyclopropane-1,1-dicarboxamide	NH O
103	N-(4-{[6,7-bis(methyloxy)quinolin-4-yl]oxy}phenyl)-N'-[2-(morpholin-4-ylmethyl)phenyl]cyclopropane-1,1-dicarboxamide	HA ON THE SECOND THE S
104	N-(4-{[6,7-bis(methyloxy)quinolin-4-yl]oxy}phenyl)-N'-phenylcyclopropane-1,1-dicarboxamide	HZ HZ
105	N-[3- (aminomethyl)phenyl]-N'- (4-{[6,7- bis(methyloxy)quinolin-4- yl]oxy}phenyl)cyclopropa ne-1,1-dicarboxamide	NH ₀ NH ₀ NH _N
106	N-(4-{[6,7-bis(methyloxy)quinolin-4-yl]oxy}phenyl)-N'-[3-(piperidin-1-ylmethyl)phenyl]cyclopropane-1,1-dicarboxamide	NH ON NH

Table 2

Entry	Name	Structure
107	N-(4-{[6,7-bis(methyloxy)quinolin-4-yl]oxy}phenyl)-N'-[3-(pyrrolidin-1-ylmethyl)phenyl]cyclopropane-1,1-dicarboxamide	NH ON

- 106. A pharmaceutical composition comprising a compound according to any one of claims 1 105 and a pharmaceutically acceptable carrier.
- 107. A metabolite of the compound or the pharmaceutical composition according to any one of claims 1 106.
- 108. A method of modulating the *in vivo* activity of a kinase, the method comprising administering to a subject an effective amount of the compound or the pharmaceutical composition according to any of claims 1 105.
- 109. The method according to claim 108, wherein modulating the *in vivo* activity of the kinase comprises inhibition of said kinase.
- 110. The method according to claim 108, wherein the kinase is at least one of c-Met, KDR, c-Kit, flt-3, and flt-4.
- 111. The method according to claim 110, wherein the kinase is c-Met.
- 112. A method of treating diseases or disorders associated with uncontrolled, abnormal, and/or unwanted cellular activities, the method comprising administering, to a mammal in need thereof, a therapeutically effective amount of the compound or the pharmaceutical composition as described in any one of claims 1 106.
- 113. A method of screening for a modulator of a kinase, said kinase selected from c-Met, KDR, c-Kit, flt-3, and flt-4, the method comprising combining a compound according to any one of claims 1 105, and at least one candidate agent and determining the effect of the candidate agent on the activity of said kinase.

114. A method of inhibiting proliferative activity in a cell, the method comprising administering an effective amount of a composition comprising a compound according any one of claims 1 - 105 to a cell or a plurality of cells.

115. A process for preparing a compound of Formula XXI,

$$(R^{1})_{0-4}$$
 R^{70}
 R^{70}
 R^{70}

comprising reaction of a compound of Formula XXII, with a compound of Formula XXIII

$$(R^1)_{0-4}$$
 R^{70}
 R^{70}
 R^{70}
 R^{70}
 R^{70}
 R^{70}
 R^{70}
 R^{70}
 R^{70}

wherein,

each R^1 is independently selected from halogen, $-OR^3$, $-NO_2$, $-NH_2$, $-NR^3R^3$, $-D-R^{50}$ and optionally substituted C_{1-6} alkyl;

 R^{70} is selected from -H, halogen, $-OR^3$, $-S(O)_{0-2}R^3$, $-NO_2$, $-NH_2$, $-NR^3R^3$, and optionally substituted C_{1-6} alkyl;

J is selected from =N-, =C(H)-, =C(halogen)-, and =C(CN)-;

Z is selected from $-S(O)_{0-2}$, -O-, and $-NR^5$ -;

each R^5 is independently selected from -H, optionally substituted C_{1-6} alkyl, optionally substituted aryl, and optionally substituted aryl C_{1-6} alkyl;

Ar is either a five- to ten-membered arylene or a five- to ten-membered heteroarylene containing between one and three heteroatoms;

 R^2 is selected from -H, halogen, trihalomethyl, -CN, -NO₂, -NH₂, -OR³, -NR³R³, -S(O)₀₋₂R³, -SO₂NR³R³, -CO₂R³, -C(O)NR³R³, -N(R³)SO₂R³, -N(R³)CO₂R³, -N(R³)CO₂R³, and optionally substituted C₁₋₆alkyl;

each R^3 is independently selected from -H, -Si(R^5)(R^5) R^5 , optionally substituted lower alkyl, optionally substituted aryl, optionally substituted arylalkyl, and optionally substituted heteroarylalkyl;

two R³, together with the nitrogen to which they are attached, form a four- to seven-membered heteroalicyclic, said four- to seven-membered heteroalicyclic optionally containing one additional heteroatom; when one said additional heteroatom is a nitrogen, then said nitrogen is optionally substituted with a group selected from -H, trihalomethyl, -SO₂R⁵, -SO₂NR⁵R⁵, -CO₂R⁵, -C(O)NR⁵R⁵, -C(O)R⁵, and optionally substituted lower alkyl;

B is selected from absent, $-N(R^{13})$ -, $-N(SO_2R^{13})$ -, -O-, $-S(O)_{0-2}$ -, and -C(=O)-;

L is selected from absent, $-C(=S)N(R^{13})$ -, $-C(=NR^{14})N(R^{13})$ -, $-SO_2N(R^{13})$ -, $-SO_2$ -, $-C(=O)N(R^{13})$ -, $-N(R^{13})$ -, $-C(=O)C_{1-2}$ alkyl $N(R^{13})$ -, $-N(R^{13})C_{1-2}$ alkylN(=O)-, $-C(=O)C_{0-1}$ alkylN(=O)-, $-C(=O)C_{0-1}$ alkylN(=O)-, $-C(=O)C_{0-1}$ alkylN(=O)-, and an optionally substituted four- to six-membered heterocyclyl containing between one and three annular heteroatoms and comprising at least one nitrogen;

T is selected from -H, -R¹³, -C₀₋₄alkyl, -C₀₋₄alkylQ, -OC₀₋₄alkylQ, -C₀₋₄alkylQ, -C₀₋₄alkylQ, -C₀₋₄alkylQ, -C₀₋₄alkylQ, -C₀₋₄alkylQ, and -C(=O)N(R¹³)C₀₋₄alkylQ, wherein each of the aforementioned C₀₋₄alkyl is optionally substituted;

Q is a five- to ten-membered ring system, optionally substituted with between zero and four of R^{20} ;

each R^{20} is independently selected from -H, halogen, trihalomethyl, -CN, -NO₂, -NH₂, -OR³, -NR³R³, -S(O)₀₋₂R³, -SO₂NR³R³, -CO₂R³, -C(O)NR³R³, -N(R³)SO₂R³, -N(R³)C(O)R³, -N(R³)CO₂R³, -C(O)R³, optionally substituted C_{1-6} alkyl, optionally substituted aryl, optionally substituted heterocyclyl, and optionally substituted heterocyclyl C_{1-6} alkyl;

two of R²⁰, together with the atom or atoms to which they are attached, combine to form an optionally substituted three- to seven-membered heteroalicyclic, said optionally substituted three- to seven-membered heteroalicyclic either spiro- to Q or fused to Q;

D is selected from -O-, -S(O)₀₋₂-, and -NR¹⁵-;

 R^{50} is either R^3 , or according to formula **XXIV**;

$$(X^{1})_{m}$$
 $(X^{3})_{n}$ $(X^{1})_{p}$

XXIV

wherein X^1 , X^2 , and optionally X^3 , represent the atoms of a saturated bridged ring system, said saturated bridged ring system comprising up to four annular heteroatoms represented by any of X^1 , X^2 , and X^3 ; wherein,

each X^1 is independently selected from $-C(R^6)R^7$ -, -O-, $-S(O)_{0-2}$ -, and $-NR^8$ -;

each X^2 is independently an optionally substituted bridgehead methine or a bridgehead nitrogen;

each X^3 is independently selected from $-C(R^6)R^7$ -, -O-, $-S(O)_{0-2}$ -, and $-NR^8$ -;

Y is either:

an optionally substituted $C_{1\text{-}6}$ alkylene linker, between D and either 1) any annular atom of the saturated bridged ring system, except X^2 when X^2 is a bridgehead nitrogen, or 2) any heteroatom, represented by any of R^6 or R^7 ; provided there are at least two carbon atoms between D and any annular heteroatom of the saturated bridged ring system or any heteroatom represented by any of R^6 or R^7 ;

or Y is absent, when Y is absent, said saturated bridged ring system, is directly attached to D via an annular carbon of said saturated bridged ring system, unless D is -SO₂-, in which case said saturated bridged ring system, is directly attached to D via an any annular atom of said saturated bridged ring system;

m and p are each independently one to four;

n is zero to two, when n is zero, then there is a single bond between the two bridgehead X^2 's;

 R^6 and R^7 are each independently selected from -H, halogen, trihalomethyl, -CN, -NH₂, -NO₂, -OR³, -NR³R³, -S(O)₀₋₂R³, -SO₂NR³R³, -CO₂R³, -C(O)NR³R³, -N(R³)SO₂R³, -N(R³)C(O)R³, -NCO₂R³, -C(O)R³, optionally substituted C₁₋₆alkyl, optionally substituted

aryl, optionally substituted aryl C_{1-6} alkyl, optionally substituted heterocyclyl a C_{1-6} lkyl, and a bond to either Y or D; or

R⁶ and R⁷, when taken together are oxo; or

R⁶ and R⁷, when taken together with a common carbon to which they are attached, form a optionally substituted three- to seven-membered spirocyclyl, said optionally substituted three- to seven-membered spirocyclyl optionally containing at least one additional annular heteroatom selected from N, O, S, and P;

 R^8 is selected from $-R^3$, Y, $-SO_2NR^3R^3$, $-CO_2R^3$, $-C(O)NR^3R^3$, $-SO_2R^3$, and $-C(O)R^3$;

 R^{13} is selected from -H, -C(=O) R^3 , -C(=O)O R^3 , -C(=O)S R^3 , -SO₂ R^3 , -C(=O)N(R^3) R^3 , and optionally substituted C₁₋₆alkyl;

two R¹³, together with the atom or atoms to which they are attached, can combine to form a heteroalicyclic optionally substituted with between one and four of R⁶⁰, said heteroalicyclic comprising up to four annular heteroatoms, and said heteroalicyclic optionally comprising an aryl or heteroaryl fused thereto, in which case said aryl or heteroaryl is optionally substituted with an additional one to four of R⁶⁰;

 R^{14} is selected from -H, -NO₂, -NH₂, -N(R^3) R^3 , -CN, -OR³, optionally substituted $C_{1\text{-}6}$ alkyl, optionally substituted heteroalicyclyl $C_{1\text{-}6}$ alkyl, optionally substituted aryl, optionally substituted aryl $C_{1\text{-}6}$ alkyl and optionally substituted heteroalicyclic;

 R^{15} is a group $-M^1-M^2$, wherein M^1 is selected from absent, $-C(=S)N(R^{13})$ -, $-C(=NR^{14})N(R^{13})$ -, $-SO_2N(R^{13})$ -, $-SO_2$ -, $-C(=O)N(R^{13})$ -, $-C(=O)C(=O)N(R^{13})$ -, $-C_{0-4}$ alkylene-, -C(=O)-, and an optionally substituted four to six-membered heterocyclyl containing between one and three heteroatoms but comprising at least one nitrogen; and M^2 is selected from -H, $-C_{0-6}$ alkyl, alkoxy, $-C(=O)C_{0-4}$ alkylQ, $-C_{0-4}$ alkylQ, $-OC_{0-4}$ alkylQ-, $-N(R^{13})C_{0-4}$ alkylQ-, and $-C(=O)N(R^{13})C_{0-4}$ alkylQ;

 R^{60} is selected from -H, halogen, trihalomethyl, -CN, -NO₂, -NH₂, -OR³, -NR³R³, -S(O)₀₋₂R³, -SO₂NR³R³, -CO₂R³, -C(O)NR³R³, -N(R³)SO₂R³, -N(R³)C(O)R³, -N(R³)CO₂R³, -C(O)R³, optionally substituted C_{1-6} alkyl, optionally substituted aryl, optionally substituted heteroaryl C_{1-6} alkyl, and optionally substituted aryl C_{1-6} alkyl;

two of R⁶⁰, when attached to a non-aromatic carbon, can be oxo;

P¹ is a suitable leaving group; and

 P^2 is selected from -H, a metal, and a group removed *in-situ* when combining **XXII** and **XXIII** to make **XXI**.

- 116. The process according to claim 115, wherein Ar is *para*-phenylene as defined by the substitution pattern of -Z- and -B-L-T about said phenylene.
- 117. The process according to claim 116, wherein Z is either -O- or -NR⁵-.
- 118. The process according to claim 117, wherein -B-L-T is selected from the following:

R ¹³ R ¹³ Q Q Q Q Q Q Q Q Q Q Q Q Q Q Q Q Q Q	R ¹³ R ¹³ Q O-3 Q	$ \begin{array}{c c} & & \\$
$\begin{array}{c c} & & & \\ & & \\ & & & \\ & & & \\ & & & \\ & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ &$	N Q Q	R ¹³ Q Q Q Q Q Q Q Q Q
R ¹³ N Q Q Q Q Q Q Q Q Q Q Q Q Q Q Q Q Q Q	$ \begin{array}{c} $	$ \begin{array}{c c} R^{13} \\ N \\ N \\ V \end{array} $ $ \begin{array}{c} M \\ V_{0-2} \end{array} $
R ¹³ R ¹³ I Q Q Q Q Q Q Q Q Q Q Q Q Q Q Q Q Q Q	R ¹³ 0-4 Q	R ¹³ O-1 O-3 O
$ \begin{array}{c c} & R^{13} \\ & N \\ & Q \end{array} $	$ \begin{array}{c} & R^{13} \\ & N \\ & N \\ & O_{0-3} \end{array} $	O O O O O O O O O O O O O O O O O O O
O O O 1-3 S N Q R ¹³	$ \begin{array}{c} O \\ \downarrow \\ O \\ \downarrow \\ O \end{array} $ $ \begin{array}{c} O \\ \downarrow \\ O \\ O \\ O \\ O \\ O \end{array} $	O

Q ()0-3 O R13	() 1-2 () 0-3 Q N N R ¹³	Q N N R ¹³
R ¹³ R ¹³ I Q N N O ₀₋₄	R ¹³ R ¹³ Q Q	$\begin{array}{c} \left(\begin{array}{c} \left(\begin{array}{c} 1 \end{array} \right)^{1-2} \\ \left(\begin{array}{c} N \end{array} \right)^{N} \end{array} \right)^{Q} \end{array}$
$ \begin{array}{c c} & & \\$	N N R ¹³	$Q \xrightarrow{N \longrightarrow N} R^{13}$
$ \begin{array}{c c} R^{13} & & \\ N & & \\ N & & \\ 0 & & \\ \end{array} $	R ¹³ Q Q	R ¹³ () Q Q O N S N O O
R ¹³ () ₀₋₃ Q SH	R ¹³ () ₀₋₃ OH	R ¹³ () ₀₋₃ R ¹³ O H
N N R13	R ¹³ N O O R ¹³	N 10-2
O O O 1-3 N E Q	0 s) ₀₋₄ 0 s) ₀₋₄ 0 s) ₀₋₄	O O R ¹³ N Q R ¹³ O Q
R ¹³ O C C C C C C C C C C C C C C C C C C	R ¹³ R ¹³ I O-3	R ¹³ N O N O N O O R ³

wherein Q, R^{20} , and R^{13} are as defined above; each E is selected from -O-, -N(R^{13})-, -CH₂, and -S(O)₀₋₂-; M is selected from -O-, -N(R^{13})-, -CH₂-, and -C(=O)N(R^{13})-; each V is independently either =N- or =C(H)-; each methylene in any of the above formulae is independently optionally substituted with R^{25} ; and R^{25} is selected from halogen, trihalomethyl, -CN, -NO₂, -NH₂, -OR³, -NR³R³, -S(O)₀₋₂R³, -SO₂NR³R³, -CO₂R³, -C(O)NR³R³, -N(R³)SO₂R³, -N(R³)C(O)R³, -N(R³)CO₂R³, -C(O)R³, optionally substituted aryl, optionally substituted aryl C₁₋₆alkyl, heteroaryl C₁₋₆alkyl, and optionally substituted C₁₋₆alkyl; two of R^{25} , together with the carbon or carbons to which they are attached, can combine to form an optionally substituted three- to seven-membered alicyclic or heteroalicyclic; two of R^{25} on a single carbon can be oxo.

- 119. The process according to claim 118, wherein there is one of R^1 that is -D- R^{50} and another of R^1 that is -OR^{3a}.
- 120. The process according to claim 119, wherein D is -O-.
- 121. The process according to claim 120, wherein -O-R⁵⁰ and -OR^{3a} are interchangeably located at the 6-position and 7-position of the quinazoline or quinoline according to Formula **XXI**.
- 122. The process according to claim 121, wherein $-OR^{3a}$ is selected from -OH, $-OSi(R^5)(R^5)R^5$, and optionally substituted $-OC_{1-6}$ alkyl.
- 123. The process according to claim 122, wherein J is =N- or =C(H)-.
- 124. The process according to claim 123, wherein -B-L-T is selected from:

wherein Q, R^{20} , R^{13} , E, and R^{60} are as defined above; each methylene in any of the above formulae, other than those in a depicted ring, is independently optionally substituted with R^{25} ; and R^{25} is selected from halogen, trihalomethyl, oxo, -CN, -NO₂, -NH₂, -OR³, -NR³R³, -S(O)₀₋₂R³, -SO₂NR³R³, -CO₂R³, -C(O)NR³R³, -N(R³)SO₂R³, -N(R³)C(O)R³, -N(R³)CO₂R³, -C(O)R³, optionally substituted aryl, optionally substituted aryl C₁₋₆alkyl, heteroaryl C₁₋₆alkyl, and optionally substituted C₁₋₆alkyl; two of R^{25} , together with the carbon or carbons to which they are attached, can combine to form a three- to seven-membered optionally substituted alicyclic or heteroalicyclic.

125. The process according to claim 124, wherein Q is selected from the following three formula:

$$(R^{20})_{0-4}$$
 $(R^{20})_{0-4}$

wherein R²⁰ is defined as above, and P is a five- to seven-membered ring, including the two shared carbons of the aromatic ring to which P is fused, P optionally containing between one and three heteroatoms.

126. The process according to claim 125, wherein -B-L-T is either of formula **XXV** or formula **XXVI**,

wherein R^{20} is defined as above; G is either an optionally substituted cycloalkyl or an optionally substituted heteroalicyclic; each R^{30} is independently selected from halogen, trihalomethyl, -CN, -NO₂, -NH₂, -OR³, -NR³R³, -S(O)₀₋₂R³, -SO₂NR³R³, -CO₂R³, -C(O)NR³R³, -N(R³)SO₂R³, -N(R³)C(O)R³, -N(R³)CO₂R³, -C(O)R³, and optionally substituted C_{1-6} alkyl; and R^{3a} and R^{3b} are each independently selected from -H and optionally substituted C_{1-6} alkyl.

127. The process according to claim 126, wherein a compound of formula **XXIIa** is combined with a compound of formula **XXIIIa** to make a compound of formula **XXIIa**,

wherein -B-L-T, Z, J, R^{50} , and R^2 are as defined above; R^{70} is selected from -H, -NO₂, -NH₂, and -NR³R³; provided when Z is -N(R⁵)- that R^5 is selected from -H, C₁₋₃alkyl, and aryl C₁₋₃alkyl; P^1 is selected from halogen, optionally substituted alkyl-S(O)₀₋₂-, optionally substituted arylsulfonate, optionally substituted alkylsulfonate, a group containing boron, an azide, a group containing phosphorus, and a metal; and P^2 is selected from -H and a metal.

- 128. The process according to claim 127, wherein P² is selected from -H, lithium, sodium, potassium, cesium, copper, palladium, and titanium.
- 129. The process according to claim 128, wherein Z is -O-.

130. The process according to claim 129, wherein P¹ is selected from chlorine, bromine, a toluene sulfonate, and trifluoromethansulfonate.

- 131. The process according to claim 130, wherein R^{70} is -H.
- 132. The process according to claim 131, wherein J is =C(H)-.
- 133. The process according to claim 132, wherein R^2 is selected from C_{1-6} alkyl, perfluoro C_{1-6} alkyl, and halogen.
- 134. The process according to claim 133, wherein **XXIIa** and **XXIIIa** are heated together, optionally with a base, optionally with microwave radiation, to form **XXIa**.
- 135. The process according to claim 134, wherein the base is selected from an organic base, an inorganic base, and a combination of an organic base and an inorganic base.
- 136. The process according to claim 135, wherein the base is selected from 2,6-lutidine, 4-N,N-dimethylaminopyridine, and a metal carbonate.
- 137. The process according to claim 136, wherein **XXIIa** and **XXIIIa** are heated together in a solvent with said base, at between about 40°C and 200°C for between about one hour and twenty-four hours to form **XXIa**.
- 138. The process according to claim 137, wherein the solvent is an organic solvent.
- 139. The process according to claim 138, wherein one molar equivalent of **XXIIa** is combined with between about one quarter and four molar equivalents of **XXIIIa**.
- 140. The process according to claim 139, wherein one molar equivalent of **XXIIa** is combined with more than one but less than two molar equivalents of **XXIIIa**.
- 141. The process according to claim 140, wherein **XXIIa** is combined with **XXIIIa** and said base in an aromatic solvent to form a mixture, and said mixture is heated to between about 100°C and 200°C for between about one and ten hours to form **Ia**.
- 142. The process according to claim 141, wherein the aromatic solvent is an optionally substituted benzene.

143. The process according to claim 142, wherein the aromatic solvent is bromobenzene.

- 144. The process according to claim 143, wherein the base is 4-N,N-dimethylaminopyridine.
- 145. The process according to claim 144, wherein said mixture is heated to reflux for between about three and seven hours.
- 146. The process according to claim 145, wherein said mixture is heated to reflux for between about four and six hours.
- 147. The process according to claim 140, wherein **XXIIa** is combined with **XXIIIa** and said base in a non-aromatic solvent to form a mixture, and said mixture is heated to between about 40°C and 100°C for between about one and twenty hours to form **XXIa**.
- 148. The process according to claim 147, wherein the non-aromatic solvent comprises a functional group selected from an amide, and ether, a nitrile, a halide, an ester, an amine, and a ketone.
- 149. The process according to claim 148, wherein the non-aromatic solvent is N,N-dimethylacetamide.
- 150. The process according to claim 149, wherein the base is potassium carbonate.
- 151. The process according to claim 150, wherein said mixture is heated to about 50°C between about ten and twenty hours.
- 152. The process according to claim 151, wherein the aromatic solvent is an optionally substituted pyridine.
- 153. The process according to claim 152, wherein the aromatic solvent is 2,6-lutidine.
- 154. The process according to claim 153, wherein the base is 2,6-lutidine.
- 155. The process according to claim 154, wherein said mixture is heated to reflux for between about three and seven hours.

156. The process according to claim 155, wherein said mixture is heated to reflux for between about four and six hours.

- 157. The process according to claim 139, wherein one molar equivalent of **XXIIIa** is combined with more than one but less than two molar equivalents of **XXIIa**.
- 158. The process according to claim 157, wherein **XXIIa** is combined with **XXIIIa** and said base in an aromatic solvent to form a mixture, and said mixture is heated to between about 100°C and 200°C for between about ten and twenty hours to form **XXIa**.
- 159. The process according to claim 158, wherein the aromatic solvent is an optionally substituted pyridine.
- 160. The process according to claim 159, wherein the aromatic solvent is 2,6-lutidine.
- 161. The process according to claim 160, wherein the base is 2,6-lutidine.
- 162. The process according to claim 161, wherein said mixture is heated to between about 150°C and 200°C for between about fifteen and twenty hours.
- 163. The process according to any of claims 134 162, wherein a compound of formula **XXIIb** is substituted for the compound of formula **XXIIIa**, and either a compound of formula **XXIIIb** or a compound of formula **XXIIIa**, in order to make a compound of formula **XXIIb** or a compound of formula **XXIIb**, respectively,

$$R^{50}$$

XXIb

wherein J, R⁵⁰, R²⁰ and R² are as defined above.

- 164. The process according to claim 163, wherein R², if present, is halogen.
- 165. The process according to claim 164, wherein R², if present, is fluorine.
- 166. The process according to claim 165, wherein R^2 , if present, is up to two fluorines ortho to the oxygen of the phenylene to which R^2 is attached.
- 167. The process according to claim 115, used to make a compound listed in either Table 1 or Table 2.
- 168. The process according to any of claims 115 167, further comprising converting said compound to a pharmaceutically acceptable salt, hydrate, or prodrug thereof.

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For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) Title: C-MET MODULATORS AND METHODS OF USE

(57) Abstract: The present invention provides compounds for modulating protein kinase enzymatic activity for modulating cellular activities such as proliferation, differentiation, programmed cell death, migration and chemoinvasion. More specifically, the invention provides quinazolines and quinolines which inhibit, regulate and/or modulate kinase receptor, particularly c-Met, KDR, c-Kit, flt-3 and flt-4, signal transduction pathways related to the changes in cellular activities as mentioned above, compositions which contain these compounds, and methods of using them to treat kinase-dependent diseases and conditions. The present invention also provides methods for making compounds as mentioned above, and compositions which contain these compounds.



INTERNATIONAL SEARCH REPORT

International application No.
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A. CLAS IPC(7)					
US CL	US CL : 514/312, 235.2, 253, 266.2, 266.3; 544/128, 235, 238, 284, 293, 363, 405.				
	According to International Patent Classification (IPC) or to both national classification and IPC				
B. FIEL	DS SEARCHED				
	cumentation searched (classification system followed 14/312, 235.2, 253, 266.2, 266.3; 544/128, 235, 238				
Documentation	on searched other than minimum documentation to the	extent that such documents are included in	the fields searched		
Electronic da CAPLUS and	ta base consulted during the international search (namd EAST	e of data base and, where practicable, sear	ch terms used)		
C. DOCI	UMENTS CONSIDERED TO BE RELEVANT				
Category *	Citation of document, with indication, where a	100	Relevant to claim No.		
Α	6,143,764 (KUBO et. al.) 07 November 2000 (07.1	1.2000), columns 14-18.	45 and 105		
	·				
A	US 5,480,883 (SPADA et. al.) 02 January 1996 (02	.01.1996), columns 55-58.	45 and 105		
A	WO 95/15758 (RHONE-POULENC RORER PHAR (15.06.1995), page 15.	RMACEUTICAL INC.) 15 June 1995	45 and 105		
A	WO 97/17329 (KIRIN BEER KABUSHIKI KAISH.	A) 15 May 1997 (15.05.1997), page 30.	45 and 105		
Further	documents are listed in the continuation of Box C.	See patent family annex.			
* Si	pecial categories of cited documents:	"T" later document published after the inter			
	defining the general state of the art which is not considered to be lar relevance	date and not in conflict with the application principle or theory underlying the investigation.	ntion		
	plication or patent published on or after the international filing date	"X" document of particular relevance; the c considered novel or cannot be consider when the document is taken alone			
"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)		"Y" document of particular relevance; the c considered to involve an inventive step combined with one or more other such	when the document is		
"O" document	referring to an oral disclosure, use, exhibition or other means	being obvious to a person skilled in the			
	published prior to the international filing date but later than the ate claimed	"&" document member of the same patent f	amily		
	etual completion of the international search	Date of mailing of the international searce 0.6. APR 2005	h report		
	05 (19.03.2005) iiling address of the ISA/US	Authorized officer			
Mai	1 Stop PCT, Attn: ISA/US	James O Wilson /), 16 m.		
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Form PCT/ISA/210 (second sheet) (January 2004)

INTERNATIONAL SEARCH REPORT

International application No. PCT/US04/31523

ategory *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim I
A	OGITA, H. et. al., Synthesis and StructureActivity Relationship of Diarylamide Urea Derivatives as Selective Inhibitors of the Proliferation of Human Coronary Artery Smooth Muscle Cells. Bioorg. & Med. Chem., 2002, Vol. 10, No. 6, pp. 1865-1871.	45 and 105
A	BOSCHELLI, D.H. et. al., Synthesis and Src Kinase Inhibitory Activity of a Series of 4-Phenylamino-3-quinolinecarbonitriles. J. Med. Chem., 2001, Vol. 44, No. 5, pp. 822-833.	45 and 105
i		
	·	
j		
		·

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US04/31523

_	No. II	Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)
This i	nternati	onal search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:
1.		Claims Nos.: because they relate to subject matter not required to be searched by this Authority, namely:
2.	\boxtimes	Claims Nos.: 1-44 and 46-104 because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically: Please See Continuation Sheet
3.		Claims Nos.: because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).
Box 1	No. III	Observations where unity of invention is lacking (Continuation of item 3 of first sheet)
This I	nternati	onal Searching Authority found multiple inventions in this international application, as follows:
1. 2.		As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims. As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite
3.		payment of any additional fee. As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:
4.	□	No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:
Rema	rk on P	The additional search fees were accompanied by the applicant's protest. No protest accompanied the payment of additional search fees.

Form PCT/ISA/210 (continuation of first sheet(2)) (January 2004)

INTERNATIONAL SEARCH REPORT International application No. PCT/US04/31523

Continuation of Box II Reason 2:

Claim 1 recites limitations that are either not realistic or inconsistently defined. For example, when m or p > 1, and X^1 is either O or S, then there could be up to 4O's or 4S's in the bridge (i.e., -O-O-O-O-, or -S-S-S-S-). Such a ring is not realistic. Also in claim 1, X^1 can be -NR⁸-, in which R⁸ appears as a substituent on N (or a terminal group, or a monovalent group). However, the definition of R⁸ includes Y, which is a liking group (or a divalent group). Thus, when X^1 is -NR⁸, it is not clear what is substituted on N, or how X^1 is attached to X^2 (via N or R⁸).

The proviso in claim 1 (on page 298) is unclear as to which end of the G portion is attached to Ar.

Claim 2 depends on claim 1, but refers to the specification (paragraph [0033]). Therefore, it is not clear which set of compounds is intended in claim 2. Because claims 1 and 2 are unclear, no meaningful search can be carried out.

Claims 3-44 depend on claim 1, and recite subgenera derived from Formula I which is too unclear for a meaningful search.

Claim 46 recites the formula of A-B-C. In the definition of B, it is not clear which end of the linking group is attached to A, and which end attached to C. Also, the definition of R⁹ (on page 377) is unclear. Particularly, the phrase "when taken together, are either an optionally substituted alkylidene or an oxo" does not indicate which groups are taken together (i.e, R⁹, R¹⁰ and R¹¹ are taken together? Or R¹⁰ and R¹¹? Or R¹², R¹⁰ and R¹¹ are taken together?). Because claim 46 is unclear, no meaningful search can be done.

Claims 47-104 depend claim 46, and recite subgenera derived from formula A-B-C, their scopes are also too unclear for a meaningful search.